SERVING THE SCIENCE OF DIAGNOSTICS

MBS
Part of BBI Solutions

ANTIBODY SERVICES

- DEVELOPMENT
- PRODUCTION
- CHARACTERISATION

CONTENTS

INTRODUCTION

BBI Solutions, brings over 25 years of knowledge, experience, process development, and project management to our customers.

Rigorous quality standards and tight adherence to exceptional laboratory practices ensure the secure delivery of quality, well supported antibodies for a specified application. As immunoassay goals in the biotechnology and pharmaceutical industries have evolved, we have risen to the challenge to effectively develop antibodies to meet the needs of diagnostic, discovery and critical reagents for pharmacokinetic (PK) studies or anti-drug assays (ADA).

WHAT YOU CAN EXPECT FROM BBI

Knowledge & experience

The antibody technical team brings just over 25 years of deep expertise in immunology, antibody and immunoassay development to every project.

Unparalleled customer communication

Customers are informed at all project stages of the data and analysis they need to make goal-driven decisions.

Advanced screening capabilities

'MultiPure' allows customers to select clones based on specificity, sensitivity, matched pair compatibility, matrix compatibility, diversity and native recognition.

cGMP manufacturing standards

cGMP *in vitro* antibody manufacturing and custom production options to secure long term supply management.

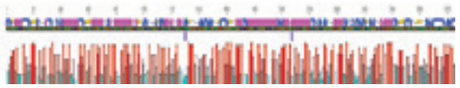
ANTIBODY DEVELOPMENT

CONSULTING & ANTIGEN REVIEW

Customers come to us with varied backgrounds and expertise, benefiting from strategising directly with a Ph.D. led technical team. By asking all the right questions up front, the team is able to not only anticipate complications, but also define a strategy to address them. Every antibody development project we do starts with a comprehensive project plan. The plan is developed by a hybridoma project manager; in collaboration with the customer, a sales representative and our technical team. It provides a roadmap for the antibody development process; identifying up front goals, timelines, reagents, strategies and contingency plans; in an effort to minimise surprises.

Thoughtful antigen development or selection is essential to developing the best antibody for your application. We provide an option to add a thorough antigen review and report, prepared by an immunologist and drawn from decades of antibody development experience.

Sample image of Secondary structure and hydrophobicity predictions from an antigen review report.



Antigen Report Features

- Sequence, features and structural analysis of the antibody target
- Linear epitope prediction
- Homology analysis
- Tertiary structural analysis of possible epitopes
- A review of reagents on the market and recommendations for use (optional)

RECOMBINANT ANTIGEN DEVELOPMENT

We offer recombinant antigen production in *E. coli* to hybridoma development customers as an antigen option. A unique value we bring to recombinant protein production is the foresight to anticipate how attributes of the recombinant protein will affect the goals of an antibody development program. Customers can expect efficient recombinant antigen development and thorough communication throughout the project.

HYBRIDOMA DEVELOPMENT

We offer over 25 years' experience in custom hybridoma development for your specified assay goal.

Our antibody development strategy focuses on developing not just any antibody, but the right antibody for a specified application. The cornerstone of that promise is our experienced technical team planning combined with our MultiPure process that generates data from large fusion screens and allows for the identification of the best performing antibody candidates prior to subcloning. If the goals of a project change during the development, we are able to use accumulated data to efficiently shift focus to meet the new goals.

Typical hybridoma development

	1-2 WEEKS	4 WEEKS	2-3 MONTHS			6-8 WEEKS	1-2 WEEKS
PHASE	PLANNING	IMMUNISATION	FUSION	GENERAL DISCOVERY REAGENTS	ADVANCED SCREENING	SUBCLONING & PRODUCTIONS	MONOCLONAL ASSAYS
ACTIVITY	Antigen review Project planning	RIMMS protocol Serum screening	Primary screening Scale-up and cryopreservation of fusion product selections Secondary screening	MultiPure technology offers novel early access to purified samples	Matched pair evolution Blocking assays Matrix evaluation	Top-ranked fusion products subcloned Monoclonal cell line cryopreservation cGMP in vitro production	Analytical characterisation of antibody(s) Fit-for-use performance evaluation
DELIVERABLES	+ Antigen analysis report + Project plan	+ Serum titre data + Boosting strategy (if needed)	+ Screening data + Banked cryo-vitals + Supernatant	+ Discovery-scale purified antibody + Biotin-labelled conjugates (optional)	+ Advanced screening report + Subcloning candidates identified	+ Screening data + Assessment of stability + Pilot production recommendations	+ Screening data + Assessment of stability + Performance characterisation report summary

MULTIPURE PROCESS

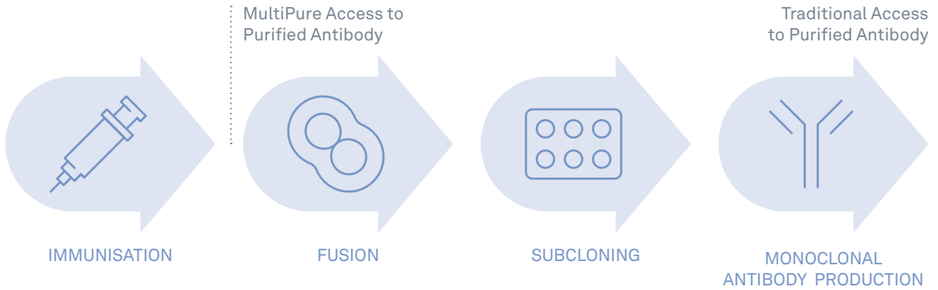
At the most critical juncture of an antibody development project, we enable our customers to efficiently and affordably select the most suitable clone for their application.

By providing purified antibody earlier in the hybridoma development process, a MultiPure clone library allows for an unprecedented opportunity to generate data including specificity, relative affinities, matched pairs and more, at just 9 weeks into your program. The typical yield for purified discovery-grade material generated from the MultiPure process is 200ug-800ug per cell line.

Advantages

+ Rapidly generates purified antibody from up to 94 fusion product supernatants at a time
+ Early evaluation of purified antibody vastly improves the selection criteria of clones based on real data
+ Normalisation of antibody concentration allows for relative affinity comparison
+ Additional plate of biotin conjugates allows for early matched-pair studies

MultiPure Technology



ADVANCED SCREENING SERVICES

Our assay development team offers a range of custom services that characterise hybridoma antibody candidates beyond the standard indirect ELISA screening. Using our proprietary MultiPure process, research grade purified antibodies are generated and can be biotinylated to normalise data and rank candidates prior to subcloning.

By integrating MultiPure samples into the antibody development process, the data generated from these assays allows customers to make more informed and efficient decisions on which hybridoma candidates to bring forward to subcloning for monoclonality and productions to support assay development.

Capabilities

+ Identification of compatible capture/detector matched pairs
+ Competitive ELISA
+ Sensitivity of detection ranking
+ Differentiation of ligand blockers and non-blockers
+ Cross-reactivity assessment
+ Matrix interference testing

PHARMACEUTICAL CUSTOMERS

At BBI Solutions, we have extensive experience developing highly sensitive and specific anti-idiotypic (anti-Id) antibodies to support the development of biotherapeutic drugs.

We have also supported many customers during the early discovery phases of development for membrane-bound protein targets and large molecule programs.

For monitoring therapeutic antibodies in clinical samples requires the ability to differentiate between administered antibody and naturally-occurring endogenous antibodies. This has become increasingly difficult as antibody biotherapeutics more closely resemble circulating human immunoglobulins. Anti-idiotypic antibodies specific for the unique variable region of the therapeutic antibody are ideal for this purpose.

Over 40% of new antibody development projects started at BBI have anti-idiotypic goals, and BBI has a 100% success rate at generating the required response to the unique specificities required to have a successful PK assay for pre-clinical and clinical studies.

Our ability to work closely with customers to clearly understand their end application, define their specific project goals and design a detailed project plan are the keys to our high success rate delivering quality anti-idiotype antibodies.

Common applications of anti-idiotypic antibodies

+ Preclinical studies of therapeutic antibody candidates
+ Anti-drug Antibodies (ADA) for clinical development
+ Pharmacokinetic (PK) assay development
+ Immune Response (IR) immunogenicity assays
+ Controls in ligand binding neutralising assays
+ Drug release assays for manufacturing

	Anti-Id Detector Ab												
Anti-Id Capture Ab	01	02	03	04	05	06	07	08	09	10	11	12	Anti-IgG (Fc)
01	1.8	2.2	2.1	2.1	1.3	2.9	1.7	0.0	0.5	1.8	0.9	1.9	2.2
02	2.3	3.1	2.7	2.2	1.7	1.0	0.3	0.1	0.1	0.4	0.2	0.4	2.8
03	1.7	2.5	2.7	1.8	1.6	0.8	0.2	0.0	0.1	0.2	0.1	0.3	2.1
04	2.8	3.0	3.1	2.1	2.1	1.1	0.1	0.1	0.0	0.1	0.0	0.1	3.2
05	0.1	0.2	0.2	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.6
06	0.5	0.3	0.4	0.2	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2
07	0.1	0.1	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
08	1.7	2.5	2.7	1.8	1.6	0.8	0.2	1.3	0.1	0.2	0.1	0.3	2.1
09	0.1	0.1	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
10	0.1	0.1	0.2	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1
11	2.4	1.9	3.2	2.3	1.9	2.1	1.4	0.1	0.3	0.9	2.0	2.5	3.5
12	1.4	3.1	3.2	2.6	1.2	0.4	0.3	0.1	0.1	0.6	0.1	2.7	3.1

Matched pair evaluation. Anti-idiotypes that perform well as both capture and detector (red circle), capture & detector pairs (purple circle), or anti-idiotype capture with anti-IgG Fc (yellow circle).

POLYCLONAL ANTIBODY DEVELOPMENT

Polyclonal antibody development can be seamlessly integrated into a project when the goal of having a matched pair is defined, or if ADA reagents are required alongside an anti-idiotype monoclonal development, or as a stand alone project. BBI offers rabbit, sheep and goat polyclonal antibody development. Collection of production bleeds begins upon consultation with the customer when the screening data indicates that the animal has generated sufficient titre and specificity for the end application. We offer purification of polyclonal sera by protein A, protein G, and antigen-specific affinity purification and Ig polishing. Having antibody samples and screening reagents already in-house, we are highly effective at compressing project timelines and accommodating budget constraints for customers.

cGMP IN VITRO

IN VITRO ANTIBODY PRODUCTION

In vitro cell culture production of monoclonal antibodies is available in roller bottles. Our cGMP facility in Portland, Maine can accommodate milligram to gram quantities of antibody. Media formulations containing low IgG fetal bovine serum, serum-free media, or animal component-free media can be used for productions upon request. Productions are designed to limit the introduction of endotoxin. Murine IgG antibodies are purified by protein A, resulting in highly pure antibody with little to no aggregation.

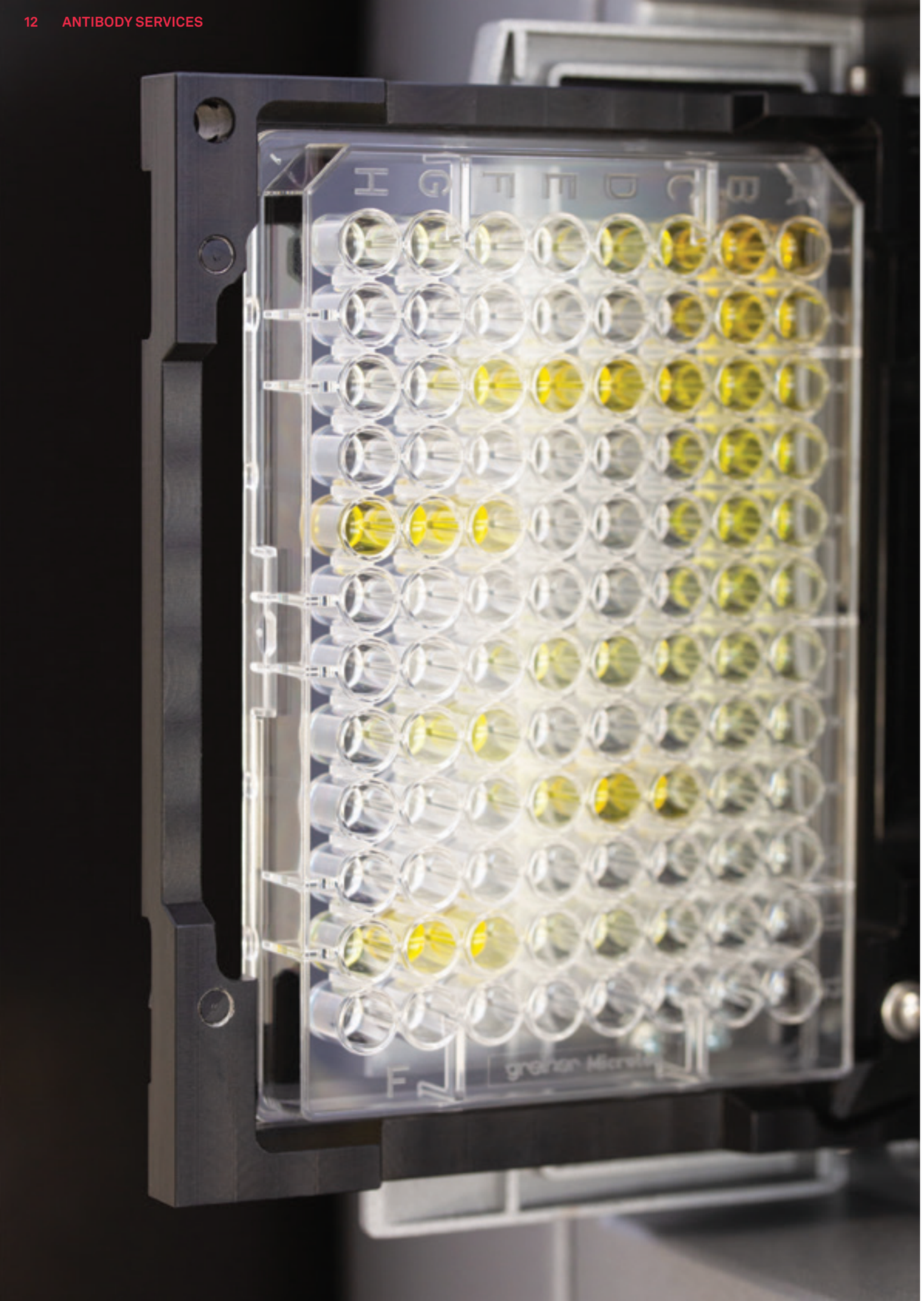
ANTIBODY PURIFICATION

We offer a wide range of cGMP purification services.

Antibody purification can be done as an extension of our monoclonal and polyclonal production offerings or as a stand alone service. Based on years of purification experience with a vast number of cell culture supernatant, ascites and serum samples, our purification team has developed optimised protocols to generate high quality antibody in quantities sufficient for early screening studies through large-scale production.

Capabilities

+ Protein A purification of mouse monoclonal cell lines with subclass-optimised binding and elution conditions
+ Protein A and Protein G purification of polyclonal serum
+ Immunoaffinity purification of polyclonal antibodies using an immobilised antigen column
+ Preparative Size Exclusion Chromatography (SEC) to remove residual aggregates, dimers and fragments and isolate monomeric IgG
+ Low endotoxin purification to generate purified antibody preparations with low EU/mg endotoxin concentrations



ANTIBODY CHARACTERISATION

BBI offers several analytical services to assess the quality and function of purified antibody productions.

These services can be integrated into the pilot production phase of a custom monoclonal antibody development project, as well as used to characterise individual batches of critical reagents that have been integrated into an immunoassay.

Available assays

Elisa	Evaluate antibody sensitivity and specificity in an immunoassay format including identification of best matched pairs and ability of antibodies to detect the antigen in a range of matrices.
Western Blot	Evaluate antibody detection and specificity in an immunoblot format.
Size exclusion chromatography (SEC)	Determine the percent purity of an antibody.
Isoelectric focusing (IEF)	Determine an antibody's isoelectric point (pI) and isoform profile.
SDS-PAGE	Analyse the integrity and purity of intact antibody.

CONJUGATION SERVICES

We offer a range of antibody conjugation services to suit your specific application. Labelling antibodies with enzymes, fluorochromes, biotin or gold generates a signal for visualisation or quantitation of the target molecule. The following conjugation services are offered as an extension of our antibody production and purification projects or as a stand-alone service:

Available conjugates

+ Biotin
+ Horseradish peroxidase (HRP)
+ Fluorescein (FITC)
+ Gold

ADDITIONAL CONTRACT SERVICES

LATERAL FLOW ASSAY DEVELOPMENT

We are able to support IVD customers in developing lateral flow assay. Whether you are looking to improve an existing assay or develop a new assay, we offer a partnership approach with customised solutions that will allow you to deliver a robust, reliable test to the global market place.

Our capabilities
Our capabilities allow us to take assay development from initial antibody screening through to final manufacture and beyond. We have over 25 years' experience developing more than 250 qualitative, semi-quantitative and quantitative assays.

Our flexible partnership
Our flexible approach means you're not locked in. A dedicated team of scientists work on your product alone. At the end of the development we hand over the design history file so that you 'own' your test. Depending on the complexity of the assay, a typical development programme for a standard IVD will work as follows:

Typical lateral flow plan

	1 MONTH	5 MONTHS	5 MONTHS	4 MONTHS		
PHASE	Proof of principle	Feasibility	Optimisation and characterisation	Validation	Manufacture	Product validation
ACTIVITY	Exploration of initial idea and theoretical viability	Collating customer requirements and investigation of formulations and processes	Characterisation and selection of final materials, formulation and processes. Transfer to manufacture	Full verification and validation of manufacturing processes to ensure assay robustness	Opportunity to implement manual, semi automated or automated solutions (scale dependent)	Plus additional consultation services available
DELIVERABLES	+ Clear pathway identified	+ A prototype assay	+ An optimised assay and pilot batches	+ Validation batches and product claims	+ Routine manufacture	+ Additional consultation

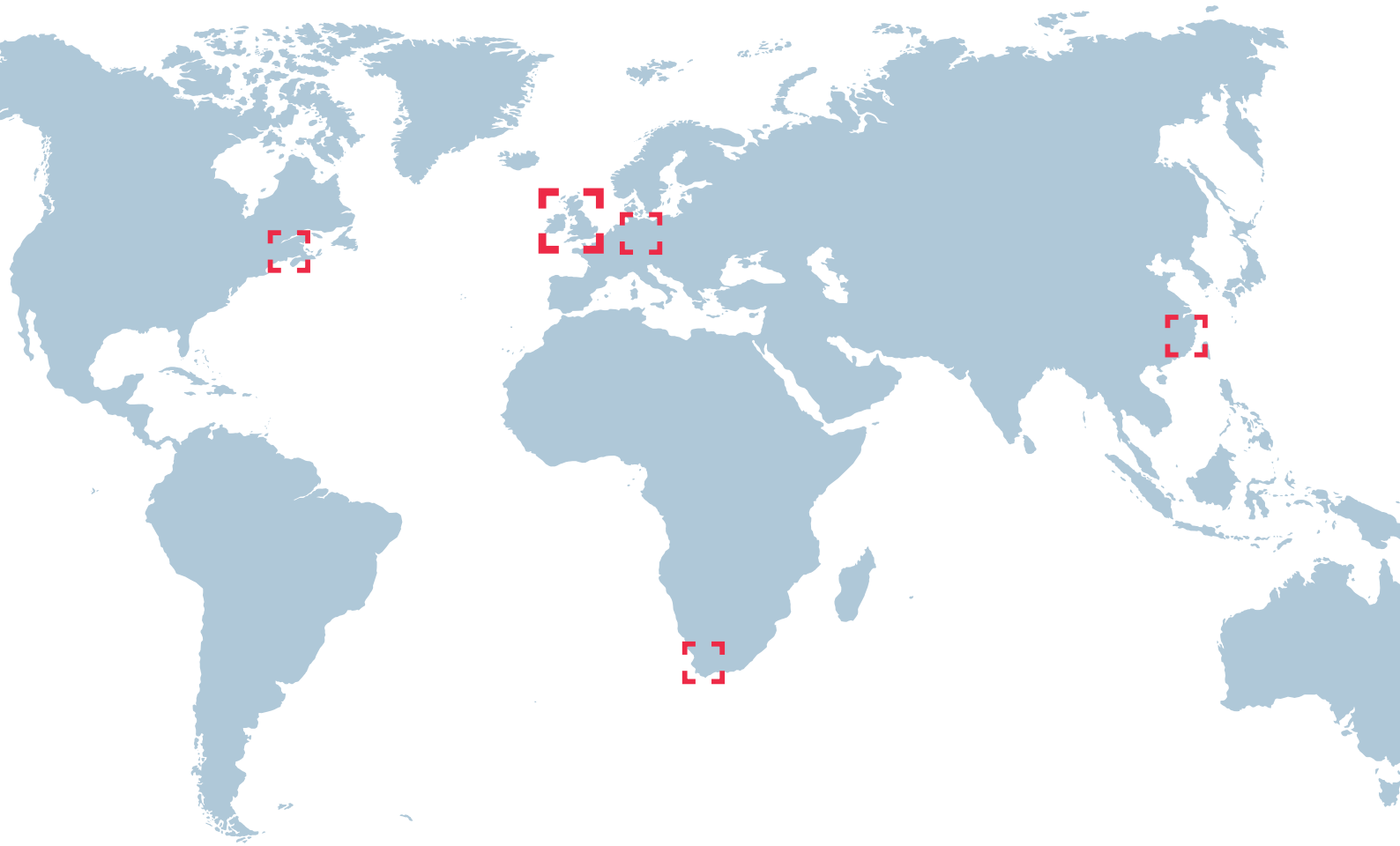
NORAUM™ DX SMARTPHONE DIAGNOSTIC READER

Developing a lateral flow test?
Make it smarter. Mobile health (mHealth) technology is growing exponentially, creating new opportunities for pharmaceutical and diagnostic companies to shape the future of digital healthcare. Recognising the increasing convergence of mobile phone disruption within point of care testing and the shift towards decentralised healthcare, BBI Solutions acquired leading smartphone diagnostics specialist, Novarum™ DX, in late 2016.

What does the Novarum smartphone technology offer?
Novarum leverages mobile phone connectivity and intuitive app development to transform a smartphone into a diagnostic reader, to support disease diagnosis, tracking and epidemiology. Mobile phones compensate for a lack of physical infrastructure, particularly for populations living in resource poor setting or remote environments. Testing can be performed from the point of care, with results of lab-quality, shared securely via a mobile eco-system to healthcare practitioners online.

Key benefits

+ **Help at-risk groups** to access regular healthcare
+ **Reduce spread of disease** with early diagnosis
+ **Support technician fieldwork** with accelerated and accurate test results outside a laboratory
+ **Remote location** connection and monitoring testing



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