BIOMARKER COMMERCIALIZATION

Interreg Baltic Sea Region

EUROPEAN UNION
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Biomarker Commercialization Review Tool

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BIOMARKER COMMERCIALIZATION (BIC) REVIEW TOOL

Designed to improve communication

The BIC Review Tool is a comprehensive checklist for selection of the most promising invention for further commercialization of IVD-applicable biomarkers.

The BIC Review Tool allows an "inventors interview"-type of approach, in addition to being a checklist for Technology Transfer Offices and Researchers. It is designed to improve communication between the stakeholders involved in the commercialization process and to facilitate collaboration. The tool is therefore in a completely different format than the Biomarker Commercialization (BIC) Guide. All introductions and explanations are missing by intention since they can already be found in the BIC Guide, Best & Pitfall Practices handbook or the Regulatory Guide.

LEAD PARTNER

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WITH THE CONTRIBUTION OF THE ENTIRE BIC CONSORTIUM

For more information: biomarker.nu

BIOMARKER COMMERCIALIZATION

Inventors (name, affiliation): _____

Inventors' contact person and contact information: _____

Inventor disclosure/report code and topic (where applicable): _____

- ◯ Number of biomarkers: _____
- ◯ Name(s), synonym(s), acronym(s) and all different codes of the biomarker(s) at the different molecular levels: _____
- ◯ Disease/condition under investigation: _____
- ◯ Type of disease (e.g. infectious, congenital, cancer, occupational): _____
- ◯ Potentially applicable molecular forms for the current test:
  - ☐ DNA
  - ☐ mRNA
  - ☐ Modification of polynucleotide (e.g. post translational modification): _____
  - ☐ Protein
  - ☐ Modification of protein (e.g. glycovariant): _____
  - ☐ Metabolite
  - ☐ Other, which: _____

DESCRIPTION OF THE PLANNED IN VITRO DIAGNOSTIC (IVD) TEST

- ◯ Test type
  - ☐ Diagnostic
  - ☐ Prognostic
  - ☐ Predictive, for which therapy:
  - ☐ Screening
  - ☐ Risk/susceptibility
  - ☐ Companion diagnostics, for which drug: _____
  - ☐ Non-IVD applicable marker, specify type of use: _____
  - ☐ Other:
- ◯ Intended use/purpose of the test: _____

1 Biomarker discovery

TRL-1 BASIC PRINCIPLES OBSERVED

CLINICAL NEED

SIGNIFICANT, DOCUMENTED CLINICAL NEED

◯ Which important clinical question the test result answers:

_____

_____

◯ Who is the intended end user:

_____

◯ Does the important clinical question come from the intended end users and is it confirmed by them:

☐ Yes, documented contact(s):

_____

☐ Additional literature referral(s):

_____

☐ No

◯ How the test result expectedly affects the treatment or the outcome of the patient:

_____

STATISTICALLY SIGNIFICANT & CLINICALLY MEANINGFUL RESULTS ESTABLISHED

◯ Clinical study type

☐ Paired case-control study,

n (pairs) = _____

☐ Cohort study, n (controls) = _____

n (cases) = _____

◯ Statistically significant (p > 0.05

☐ Yes, p = _____

☐ No

◯ Difference in affected vs. healthy people, effect size, and 95 % CI: _____

◯ RR, OR or HR (where applicable): _____

◯ Is the difference large enough to convince a clinician in routine setting?

☐ Yes, no or little overlap (in healthy vs. affected); the difference is relevant to an individual patient

☐ No, significant overlap between groups

COMMERCIAL VIABILITY

TEST RESULT AFFECTS SELECTION OF TREATMENT

◯ Is there therapy existing for the disease/condition targeted?

- ☐ Yes (specify): _____
- ☐ No
- ☐ No, but the marker provides potential for drug development
- (☐ non-IVD applicable biomarker)

◯ How the test result is expected to affect the treatment of the patient:

_____

_____

_____

TEST FILLS A GAP OR OTHERWISE IMPROVES CURRENT TESTING SCHEME

◯ Is the test expected to enable detecting the disease at early stage?

- ☐ Yes, before clinical symptoms
- ☐ Yes, directly after onset of the acute disease
- ☐ No

• If no, can the disease yet be successfully treated at the time of test result?

- ☐ Yes
- ☐ No

◯ How the test expectedly improves the current testing scheme:

_____

_____

_____

FEASIBILITY & IPR

PRACTICAL ROUTINE ASSAY FEASIBLE

◯ Is the clinical concentration of the biomarker high enough to be measured by a practical routine assays?

- ☐ Yes, conc. range: _____
- ☐ No

◯ Which practical assay platform you envision for the final product: _____

◯ Which specimen types are feasible:

- ☐ Non-invasive matrices (e.g. blood, urine): _____
- ☐ Invasive matrices (e.g. CSF, biopsy):_____
- ☐ Invasive specimen is routinely taken regardless:
  - ☐ Yes
  - ☐ No, but performing the test requires one

◯ Is the biomarker stable in the (stored)clinical specimens?

- ☐ Yes, results of preliminary stability studies (e.g. freeze-thaw cycles, recovery-% etc.):

_____

- ☐ Specimen type and storage conditions: _____
- ☐ No, not tested
- ☐ No, specify: _____

◯ Is the biomarker present in fresh specimens from healthy people:

- ☐ Yes: _____
- ☐ No

◯ Does the test involve complex result interpretation?

- ☐ Yes, multiplex biomarker panel
- ☐ Yes, multiple molecular types of biomarkers
- ☐ Yes, personalized decision tree or sequential multi-parameter testing
- ☐ No

BIOMARKER OR ITS CORRELATION TO DISEASE IS A NOVEL FINDING

◯ Is/are the biomarker(s) previously known in the literature?

- ☐ No
- ☐ Yes, in the same indication (which biomarker(s)):

_____

_____

- ☐ Yes, in another indication, (which biomarker(s), which indication):

_____

_____

- ☐ If Yes, are they routinely measured in clinical settings (how and in what conc. range)?

_____

_____

2 Biomarker verification and preliminary scientific validation studies

TRL-2 PROOF OF PRINCIPLE STUDIES

CLINICAL NEED

CLINICALLY SIGNIFICANT RESULTS ESTABLISHED

◯ Description of the clinical cohort used in verification studies:

- ☐ cases: _____
- ☐ Exclusion criteria: _____
- ☐ (n) of controls = _____
- ☐ Speciment matrix = _____

◯ Is the original observation repeated with increased sample size:

- ☐ Yes, p = _____
- ☐ No, p = _____

◯ Difference in affected vs. healthy people, effect size, and 95 % CI:

_____

_____

◯ RR, OR or HR (where applicable):

_____

_____

◯ Is the magnitude of the observed difference of practical importance, i.e. clinically significant:

- ☐ Yes, how: _____

  _____
- ☐ No

◯ Have the findings been confirmed at other sites?

- ☐ Yes: _____

  _____
- ☐ No, could not be confirmed

SCIENTIFIC VALIDITY: ASSOCIATION AND SPECIFICITY TO DISEASE CONFIRMED

◯ Is the underlying biological pathway linking the biomarker to the disease known or under investigation:

- ☐ Yes: Shared molecular pathology (e.g. cellular stress) across diseases can be excluded because:

  _____

  _____
- ☐ No

COMMERCIAL VIABILITY

POSITIVE DOCUMENTED FEEDBACK FROM CLINICIANS / CLINICAL LABORATORIES

◯ What is the significant clinical question (i.e. the need) the test answers:

_____

_____

◯ Is the magnitude of the observed difference of practical importance, i.e. clinically significant:

☐ Yes, documented feedback: _____

_____

☐ Additional literature referrals: _____

_____

☐ No

LARGE TARGET POPULATION IDENTIFIED

◯ Prevalence of the disease/condition in (different) population(s):

_____

_____

◯ Who are to be tested (mark all):

☐ Entire population

☐ Specific subgroup of the population, which: _____

_____

☐ Entire affected population (with already established diagnosis)

☐ Specific population of the sick, which: _____

◯ Share amongst all sick: _____ %

☐ Newborn / children / teenagers (select)

☐ Adults with age range of:_____

☐ Elderly

☐ Female

☐ Male

☐ Specific ethnicities: _____

☐ Specific timing or other trigger: _____

◯ Contraindications for testing (which, when): _____

◯ Estimated yearly number of cases and tests for the above target group

☐ Locally: _____

☐ Internationally (specify): _____

◯ Estimated price of test: _____€

◯ Estimated maximum yearly size of the specified market (cases x €) = _____ €

◯ Is the market potential significant (profits >> patenting costs?)

☐ Yes

☐ No

FEASIBILITY & IPR

QUANTITATIVE ASSAY TECHNOLOGIES USED

◯ Assay technology(ies) used in the verification studies:

_____

_____

◯ Are the used assay technologies:

- ☐ quantitative
- ☐ target-specific
- ☐ high-throughput / up-scalable
- ☐ automatable
- ☐ currently used in routine
- ☐ sensitive (clinical concentrations fall within the linear measuring range)
- ☐ No, another assay technology to be used in prototype assay for proof-of-concept studies, which:

_____

_____

◯ Have plans and specifications been made for the prototype assay:

- ☐ Yes:
  - ☐ Reagent plan
  - ☐ Instrument plan
  - ☐ Technical specifications
- ☐ No, reason:_____

◯ Are specialized instrumentation or chemically modified reagens required in the prototype assay?

- ☐ Yes which and why:_____
- ☐ No

BIOMARKER OR ITS CORRELATION TO DISEASE IS INVENTIVE AND PATENTABLE

◯ Internal novelty and patentability survey performed:

_____

_____

◯ External novelty and patentability survey performed:

_____

_____

◯ Previous publications by inventors (incl. abstracts, posters and presentations) reviewed:

- ☐ Yes: invention not previously published by the team
- ☐ Yes: invention published and non-patentable
- ☐ No

◯ The invention is novel

- ☐ Yes, the novel features concern:
  - ☐ Singular biomarker(s)
  - ☐ Panel of biomarkers
  - ◯ Is comprehensive patent protection yet achievable?
    - ☐ Yes, strategy: _____
    - ☐ Computer algorithm
    - ☐ Sequences of binders
  - ◯ Is comprehensive patent protection yet achievable?
    - ☐ Yes, strategy: _____
    - ☐ Method of producing (instead of product)
  - ◯ Is the use of the method evident in the final product?
    - ☐ Yes, how: _____
    - ☐ No
  - ◯ Is comprehensive patent protection yet achievable?
    - ☐ Yes, strategy: _____
    - ☐ No
    - ☐ Other: _____
  - ◯ The invention is inventive:
    - ☐ Yes, the non-obvious, surprising features concern: _____
    - ☐ No

3 Development of a specific biomarker assay (prototype)

TRL-3 PROOF OF CONCEPT ASSAY ESTABLISHED

CLINICAL NEED

GOOD PRELIMINARY CLINICAL PERFORMANCE

◯ Good preliminary clinical performance

o Description of clinical specimens used in setting up the prototype assay:

- ☐ Speciment matrix: _____
- ☐ Speciment preparation: _____
- ☐ Selection criteria and (n) of cases: _____
- ☐ Selection criteria and (n) of controls: _____

◯ Results obtained with prototype correlate well with the original observations:

- ☐ Preliminary cut-off concentration used: _____
- ☐ Preliminary diagnostic sensitivity: _____ %
- ☐ Preliminary diagnostic specificity: _____ %
- ☐ Other applicable measures: _____

◯ Stability of the biomarker in the matrixes studied:

- ☐ RT: _____
- ☐ -20 ☐ C/- 70 ☐ C: _____
- ☐ Freeze-thaw cycles: _____
- ☐ Recovery-%: _____

COMMERCIAL VIABILITY

COMPETITIVE ADVANTAGE ACHIEVED

◯ Clear purpose and need for the test has been established and verified by end-users in writing:

- ☐ Yes: _____
- ☐ No, situation has changed: _____

◯ List all competing methods (commercial or under development)

- ☐ For the same target molecule (also when different molecular class): _____
- ☐ For another target molecule: _____
- ☐ A non-biomarker based test or imaging approach: _____

◯ Advances of the new test over the competing methods:

- ☐ Increased accuracy
- ☐ Earlier diagnoses
- ☐ Earlier therapeutic actions
- ☐ Improved convenience
- ☐ Decreased number of tests of procedures
- ☐ Cost-savings due to other reasons:_____
- ☐ Other: _____
- ☐ Competing methods do not exist, reason: _____

◯ Are the results of the new test comparable to the golden standard (or equivalent) approach:

- ☐ Yes, method tested against and correlation: _____
- ☐ No, not tested because: _____

_____

RISK MANAGEMENT

CLINICAL

◯ Number of false positives per each true positive (100/PPV): _____

◯ Is over-diagnostics possible? If yes, what are the consequences to a patient (especially note invasive testing or therapy steps):

- ☐ Yes: _____
- ☐ No

◯ Number of false negatives per each true negative (100/NPV): _____

◯ Is under-diagnostics possible? If yes, what are the consequences to a patient (especially note life-threatening situations):

- ☐ Yes: _____
- ☐ No

LEGAL

◯ Informed consent of patients allows commercial use (incl. patenting) of results:

- ☐ Yes
- ☐ No

◯ MTA's made allow commercial use (incl. patenting) of results:

- ☐ Yes
- ☐ No

IPR AND FTO

◯ Sufficient IP rights and FTO can be achieved:

- ☐ Yes
- ☐ No, invention non-patentable or lacks FTO: _____

FEASIBILITY & IPR

SPECIFIC AND PRACTICAL PROTOTYPE (PROOF-OF-CONCEPT ASSAY) ESTABLISHED

◯ Analytical performance (i.e. ability to correctly measure the biomarker) conforms to predefined technical specifications:

- ☐ Limit of detection: _____
- ☐ Limit of quantification: _____
- ☐ Linear measuring range: _____
  - ☐ Clinical concentrations fall within linear measuring range?
    - ☐ Yes: _____
    - ☐ No: _____
  - ☐ Hook-effect controlled?
    - ☐ Yes: _____
    - ☐ No: _____

◯ Practicability characteristics conform to predefined specifications:

- ☐ Specimens accepted: _____
- ☐ Required skills and labor in specimen preparation:
  - ☐ Low, steps: _____
  - ☐ High, steps: _____
  - ☐ Pre-analytical requirements for specimens (collection, processing, storage): _____
  - ☐ Exclusion criteria: _____
  - ☐ Total turn-around-time of assas_____

◯ Reliability characteristics conform to predefined specifications:

- ☐ Trueness of measurement (bias): _____
- ☐ Precision of measurement (repeatability, reproducibility) _____
- ☐ Recovery in spiked specimens: _____
- ☐ Interferences detected:
  - ☐ No
  - ☐ Yes: _____

FREEDOM-TO-OPERATE (FTO)

◯ In-house or IPR-free, multi-vendor commercial key components are available/can be made available economically at sufficient scale:

- ☐ Yes
- ☐ No, commercial license for following components required: _____
- ☐ No, only singular vendors exist for following components: _____
- ☐ No, following components are available only low-scale (or high-cost): _____

Describe the limiting factors and components:

_____

_____

◯ Techniques used in the prototype / proof-of-concept assay can be used without a commercial license:

- ☐ Yes
- ☐ No, commercial license is required for the following technology: _____

◯ In case of FTO hindrance, describe the geographical and temporal coverage:

_____

_____

DECISION ON PATENTING:

- ☐ Yes, patenting to be initiated
- ☐ No

Can alternative commercialization routes be considered:

- ☐ Knowledge transfer
- ☐ Material licensing
- ☐ Services-for-fee
- ☐ Database licensing
- ☐ Software licensing
- ☐ Other, specify: _____

4 Clinical performance of the prototype in laboratory settings

TRL-4 PROOF OF CONCEPT STUDIES WITH PROTOTYPE ASSAY

CLINICAL NEED

CLINICAL PERFORMANCE OBJECTIVES MET

◯ Description of the clinical cohort used in proof-of-concept studies:

- ☐ Speciment matrix: _____
- ☐ Selection criteria and (n) of cases: _____
- ☐ Exclusion criteria: _____
- ☐ (n) of controls = _____
- ☐ Are the specimens representative of the target population?
- ☐ Yes, minimal specimen picking
- ☐ No, describe the picking criteria:

_____

_____

◯ Results obtained with prototype correlate well with the condition:

AUC (in ROC analysis): _____

- ☐ Suggested cut-off value: _____
- ☐ Diagnostic sensitivity: _____ %
- ☐ Diagnostic specificity: _____ %
- ☐ Negative predictive value (NPV): _____
- ☐ Positive predictive value (PPV): _____
- ☐ Other applicable measures, e.g. relative risk ratio, hazard ratio, etc.: _____

COMMERCIAL VIABILITY

POSITIONING IN CLINICAL CARE PATHWAY CONFIRMED

◯ Clear purpose and need for the test verified by end-users in writing:

- ☐ Yes: _____
- ☐ No, feedback obtained: _____

◯ Expected positioning in the clinical care pathway:

- ☐ Stand-alone test (preceding or confirmatory tests not required)
- ☐ Add-on test; to be incorporated in existing testing sequence
  - • Preceded by following test(s): _____
  - • Followed by following test(s):_____
- ☐ Performed simultaneously with following test(s): _____
- ☐ Replaces an existing test of: _____
- ☐ Improves an existing test of:_____
- ☐ Improvements achieved: _____

◯ Intended use settings:

- ☐ Clinical laboratory
- ☐ Near-patient testing
  - ☐ Emergency (acute testing)
  - ☐ Infectious disease
  - ☐ Chronic disease
  - ☐ Other, specify: _____
- ☐ Self-testing

EVIDENCE OF HEALTH BENEFITS AND COST-EFFECTIVENESS

◯ How the test improves the patient outcome: _____

◯ How the test improves the cost-efficiency of the clinical care pathway:

- ☐ Improved diagnostic accuracy
- ☐ Decreased need of (more) expensive tests or therapies
- ☐ Other: _____
- ☐ Does not decrease costs

FEASIBILITY & IPR

PATENTING IN PROGRESS

◯ Priority year development plan followed:

- ☐ Yes, milestones met and new experimental evidence established: _____
- ☐ No, alternative plan followed:

_____

_____

- ☐ No, new evidence not established, or it does not support the patent application:

_____

◯ Patenting with sufficient scope of patent protection seems likely based on Office Actions received

- ☐ Yes
- ☐ No, specify hindrances identified: _____

◯ IPR covers all self-made changes and improvements:

- ☐ Yes
- ☐ No, specify: _____

◯ Continuing active contribution of inventors available

- ☐ Yes
- ☐ No

◯ Based on above, proceeding to international PCT phase is feasible:

- ☐ Yes
- ☐ No

5 Pre-industrial maturation phase

TRL-5 CONFIGURATION TO INDUSTRIAL APPLICATION (BETA PROTOTYPE)

TRL-6 TECHNOLOGY DEMONSTRATED IN RELEVANT ENVIRONMENT

COMMERCIAL VIABILITY

FURTHER CLINICAL EVIDENCE ACCUMULATED IN COLLABORATION WITH CLINICIANS / INDUSTRY

◯ Description of studies conducted:

- ☐ Cohort study: _____
- ☐ Retrospective randomized trial: _____
- ☐ Prospective randomized trial: _____

◯ Clinical concentrations and reference ranges

- Healthy persons: _____
- Affected persons: _____
- ☐ Are all clinical concentrations detectable by the beta prototype:
- ☐ Yes
- ☐ No, specify: _____

◯ Within-subject variation:

- ☐ Yes: _____
- ☐ No

◯ Between-subject variation:

- ☐ Yes: _____
- ☐ No

◯ Endogeneous and/or exogeneous interference encountered:

- ☐ Yes: _____
- ☐ No

◯ Cross-reacting substances:

- ☐ Yes: _____
- ☐ No

◯ What kind of feedback is obtained from the intended end users (including modifications suggested):

_____

_____

FURTHER KNOWLEDGE OF BIOMARKER BIOLOGY

◯ Are following factors of the biomarker known:

- ☐ Where it is expressed (e.g. intracellular, intra-nuclear, excreted):_____
- ☐ When and how long it is expressed: _____
- ☐ What molecular classes can be detected, which one is preferred: _____
- ☐ How many different manifestations of the molecule exists (in selected molecular class): _____
- ☐ How stable are the molecular forms in the circulation: _____
- ☐ How the fasting state, circadian rhythm, age, gender or ethnicity affects the results: _____
- ☐ Other, specify: _____

CLINICAL NEED

ASSESSMENT OF BUSINESS MODELS

◯ Considerations for establishing a start-up (select applicable):

- ☐ High degree of readiness, reasonable amount of research and product development required
- ☐ Large size and high growth rate of market; high market share can be obtained
- ☐ Low competition, few alternative solutions in sight
- ☐ Wide scope of patent protection achieved further prevents competition
- ☐ Motivated team with entrepreneurial mindset
- ☐ Sound business plan, realistic funding options available

FEASIBILITY & IPR

BETA PROTOTYPE ESTABLISHED

◯ Documented specifications, optimizations and measured performance:

- Analytical performanc
- Clinical performance