## *SYNERGIQC TRL EXTENDED DEFINITION TABLE*

**Important note for all biopharmaceutical technologies and products:**

All activities listed in TRL levels should be completed in order to rate a particular technology to this TRL level (e.g., a product is rated at TRL 4 once it completes all of the activities listed in TRL 4). If all the activities described in the TRL level are not completed, the TRL level of the technology should be one level lower.

| Level | Definition | Biomarkers | Development of molecules (New Chemical Entities: NCE) and biologics | Imaging technologies and other devices |
|---|---|---|---|---|
| **TRL 1** | **Review scientific knowledge base** | **Review of scientific knowledge base**<br>Literature review; basic principles have been observed and reported | **Review of scientific knowledge base**<br>• Literature review; basic scientific research is translated into potential principles for new technologies | **Review of scientific knowledge base**<br>• Literature review; basic scientific research is translated into potential principles for new technologies |
| **TRL 2** | **Development of hypothesis and experimental design** | **New concept or research avenues are formulated**<br>Technology maturation plan and/or grant formulated; use computer simulation if appropriate | **New concept or research avenues are formulated**<br>• Technology maturation plan and/or grant formulated; use computer simulation if appropriate | **New concept or research avenues are formulated**<br>• Technology maturation plan and/or grant formulated; use computer simulation if appropriate |
| **TRL 3** | **Analytical and experimental critical function** | **Technology to assess biomarkers is validated**<br>New putative biomarkers are identified | **Target/candidate identified and characterised**<br>• New chemical entities are synthesized<br>• Targets, hits and leads are identified<br>• Lead development<br>• Demonstrated *in vitro* activity<br>• *In vivo* proof of concepts generated | **Feasibility of concept and technologies is finalised**<br>New imaging apparatus is built, and performance validated, and imaging probes are synthesized |

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| **TRL 4** | **First experimental proof-of-concept** | **Analytical and experimental proof of principles established**<br>A set of biomarkers is tested in vitro or in vivo and data analyzed | **Candidate (lead) optimized and non-GLP *in vivo* activity and efficacy fully demonstrated**<br>• Clinical candidate generated from leads<br>• Laboratory scale (non-GMP) quantities of lead is manufactured<br>• Development of relevant (non-GMP) assays and animal model well under way<br>• Non-GLP in vivo activity (dose, route, duration, schedule) demonstrated<br>• Non-GLP toxicity, pharmacodynamics, pharmacokinetics immune response in appropriate animal models under way | **Experimental proof of concepts finalised**<br>• Images are generated with the instrument, using the "probes (imaging agents)"appropriate to the project |
| **TRL 5** | **Full validation in relevant laboratory environment** | **Component and/or systems validated in laboratory environment**<br>Biomarkers are first tested in appropriate tissues/animal models | **Advanced characterization of candidate finalized and GMP process development initialized**<br>• Develop manufacturing process amenable to GMP<br>• Completed toxicity studies<br>• Demonstrated acceptable absorption, distribution,<br>• Metabolism and Elimination (ADME) characteristics in non-GLP animal studies<br>• Minimal effective dose identified | **Instrument fully validated in relevant environment**<br>• Imaging technology is first tested and benchmarked in appropriate tissues and animal models |

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|---|---|---|---|---|
| **TRL 6** | **First tests in relevant end-user environment (pilot scale)** | **Demonstration in relevant environment**<br>Biomarkers discrimination in a first relevant human cohort (small scale) | **GMP pilot lot production, Investigational New Drug (IND) submitted and Phase I clinical trial(s)**<br>• Manufacture GMP-compliant pilot and bulk lots<br>• Prepare and submit full IND package<br>• Complete Phase I clinical trial(s) to establish initial safety, PK and immunogenicity | **First tests in relevant end-user environment (pilot scale)**<br>• Imaging technology is scaled up for human testing (a prototype is made)<br>• First assessment in humans is performed |