

IMEx dependency rules

1) Interaction detection method and interaction type

As a general rule, a direct interaction (MI:0407) **must** be showed in vitro (taxid = -1) and **must** be composed of only one to two participants.

*a) Interaction detection methods for which the interaction type **should** be direct interaction (MI:0407) when number of participants is 1 or 2 and **should** be physical association (MI:0915) when number of participants is more than 2*

- circular dichroism (MI:0016)
- electron resonance (MI:0043)
- isothermal titration calorimetry (MI:0065)
- light scattering (MI:0067)
- nuclear magnetic resonance (MI:0077)
- surface plasmon resonance and its children (MI:0107)
- X-ray crystallography and its children (MI:0114)
- intermolecular force (MI:0859)
- small angle neutron scattering (MI:0888)
- neutron fiber diffraction (MI:0891)
- neutron diffraction (MI:0893)
- electron diffraction (MI:0894)
- amplified luminescent proximity homogeneous assay (MI:0905)
- rheology measurement (MI:0938)

b) Protein complementation assay (MI:0090), saturation binding (MI:0440) and their children

The interaction type **should** only be physical association (MI:0915) independently from the number of participants.

c) Cross-linking study and its children (MI:0030) and molecular sieving (MI:0071)

The interaction type **should** be physical association (MI:0915) if the host organism is in vivo (taxid = -4), independently from the number of participants.

The interaction type **should** be direct interaction (MI:0407) if the host organism is in vitro (taxid = -1) and the interaction is composed of two participants.

d) affinity chromatography technology and its children (MI:0004)

The interaction type **should** be physical association (MI:0915) if the interaction is of type 'one bait – one prey', independently from the host organism.

The interaction type **should** be association (MI:0914) if the interaction is of type 'one bait – many preys' or 'many baits – many preys'.

*e) Interaction detection methods for which the interaction type **should** be direct interaction (MI:0407) when number of participants is 2 and **should** be physical association (MI:0915) otherwise*

- protein array (MI:0089)
- peptide array (MI:0081)
- surface plasmon resonance array (MI:0921)
- display technology (MI:0034)
- saturation binding (MI:0440)
- competitive binding (MI:0405)
- solid phase assay (MI:0892)

e) Other interaction detection methods

The following dependencies (Interaction detection method → Interaction type) are independent from the number of participants and the host organism

- MI:0406 deacetylase assay and its children -> MI:0197 deacetylation reaction
- MI:0889 acetylation assay and its children -> MI:0192 acetylation reaction
- MI:0424 protein kinase assay and its children -> MI:0217 phosphorylation reaction
- MI:0434 phosphatase assay and its children -> MI:0203 dephosphorylation reaction
- MI:0435 protease assay -> MI:0570 protein cleavage
- MI:0515 methyltransferase assay and its children -> MI:0213 methylation reaction
- MI:0697 dna directed dna polymerase assay -> MI:0701 dna strand elongation
- MI:0696 polymerase -> MI:0986 nucleic acid strand elongation
- MI:0699 rna directed dna polymerase assay -> MI:0701 dna strand elongation
- MI:0698 dna directed rna polymerase assay -> MI:0987 rna strand elongation
- MI:0700 rna directed rna polymerase assay -> MI:0987 rna strand elongation
- MI:0841 phosphotransfer assay -> MI:0844 phosphotransfer reaction
- MI:0870 demethylase assay -> MI:0871 demethylation reaction
- MI:0879 nucleoside triphosphatase assay -> MI:0881 nucleoside triphosphatase reaction
- MI:0419 gtpase assay -> MI:0883 gtpase reaction
- MI:0880 atpase assay -> MI:0882 atpase reaction
- MI:0920 ribonuclease assay -> MI:0902 rna cleavage
- MI:0406 amidation assay -> MI:0193 amidation reaction
- desoxyribonuclease assay -> MI:0572 dna cleavage
- MI:0996 deformylation assay -> MI:0199 deformylation reaction
- MI:0998 deubiquitination assay -> MI:0204 deubiquitination reaction
- MI:0999 formylation assay -> MI:0207 formylation reaction
- MI:1000 hydroxylase assay -> MI:0210 hydroxylation reaction
- MI:1001 farnesylation assay -> MI:0206 farnesylation reaction
- MI:1003 geranylgeranylation assay -> MI:0209 geranylgeranylation reaction
- MI:1002 myristoylation assay -> MI:0214 myristoylation reaction
- MI:1004 palmitoylation assay -> MI:0216 palmitoylation reaction

- MI:0997 ubiquitination assay -> MI:0220 ubiquitination reaction
- MI:1005 adp ribosylation assay -> MI:0557 adp ribosylation reaction
- MI:1006 deglycosylation assay -> MI:0558 deglycosylation reaction
- MI:1007 glycosylation assay -> MI:0559 glycosylation reaction
- MI:1008 sumoylation assay -> MI:0566 sumoylation reaction
- MI:1010 neddylation assay -> MI:0567 neddylation reaction
- MI:1009 desumoylation assay -> MI:0568 desumoylation reaction
- MI:1011 deneddylation assay -> MI:0569 deneddylation reaction
- MI:0979 oxydoreductase assay -> MI:0945 oxydoreductase activity electron transfer assay
- MI:0054 Fluorescence-activated cell sorting -> MI:0915 physical association
- MI:0991 lipid cleavage assay -> MI:0212 lipid cleavage reaction
- MI:0984 deaminase assay -> MI:0985 deamination reaction
- MI:0992 defarnesylation assay -> MI:0198 defarnesylation reaction
- MI:0993 degeranylgeranylation assay -> MI:0200 degeranylgeranylation reaction
- MI:0994 demyristoylation assay -> MI:0201 demyristoylation reaction
- MI:0995 depalmitoylation assay -> MI:0202 depalmitoylation reaction
- MI:0406 deacetylase assay and its children -> MI:0197 deacetylation reaction
- MI:0889 acetylation assay and its children -> MI:0192 acetylation reaction
- MI:0424 protein kinase assay and its children -> MI:0217 phosphorylation reaction
- MI:0434 phosphatase assay and its children -> MI:0203 dephosphorylation reaction
- MI:0435 protease assay -> MI:0570 protein cleavage
- MI:0515 methyltransferase assay and its children -> MI:0213 methylation reaction
- MI:0697 dna directed dna polymerase assay -> MI:0701 dna strand elongation
- MI:0696 polymerase -> MI:0986 nucleic acid strand elongation
- MI:0699 rna directed dna polymerase assay -> MI:0701 dna strand elongation
- MI:0698 dna directed rna polymerase assay -> MI:0987 rna strand elongation
- MI:0700 rna directed rna polymerase assay -> MI:0987 rna strand elongation
- MI:0841 phosphotransfer assay -> MI:0844 phosphotransfer reaction
- MI:0870 demethylase assay -> MI:0871 demethylation reaction
- MI:0879 nucleoside triphosphatase assay -> MI:0881 nucleoside triphosphatase reaction
- MI:0419 gtpase assay -> MI:0883 gtpase reaction
- MI:0880 atpase assay -> MI:0882 atpase reaction
- MI:0920 ribonuclease assay -> MI:0902 rna cleavage and its children
- MI:0406 amidation assay -> MI:0193 amidation reaction
- desoxyribonuclease assay -> MI:0572 dna cleavage
- MI:0996 deformylation assay -> MI:0199 deformylation reaction
- MI:0998 deubiquitination assay -> MI:0204 deubiquitination reaction
- MI:0999 formylation assay -> MI:0207 formylation reaction
- MI:1000 hydroxylase assay -> MI:0210 hydroxylation reaction
- MI:1001 farnesylation assay -> MI:0206 farnesylation reaction
- MI:1003 geranylgeranylation assay -> MI:0209 geranylgeranylation reaction
- MI:1002 myristoylation assay -> MI:0214 myristoylation reaction
- MI:1004 palmitoylation assay -> MI:0216 palmitoylation reaction

- MI:0997 ubiquitination assay -> MI:0220 ubiquitination reaction
- MI:1005 adp ribosylation assay -> MI:0557 adp ribosylation reaction
- MI:1006 deglycosylation assay -> MI:0558 deglycosylation reaction
- MI:1007 glycosylation assay -> MI:0559 glycosylation reaction
- MI:1008 sumoylation assay -> MI:0566 sumoylation reaction
- MI:1010 neddylation assay -> MI:0567 neddylation reaction
- MI:1009 desumoylation assay -> MI:0568 desumoylation reaction
- MI:1011 deneddylation assay -> MI:0569 deneddylation reaction
- MI:0979 oxydoreductase assay -> MI:0945 oxidoreductase activity electron transfer assay
- MI:0054 Fluorescence-activated cell sorting -> MI:0915 physical association
- MI:0991 lipid cleavage assay -> MI:0212 lipid cleavage reaction
- MI:0984 deaminase assay -> MI:0985 deamination reaction
- MI:0992 defarnesylation assay -> MI:0198 defarnesylation reaction
- MI:0993 degeranylgeranylation assay -> MI:0200 degeranylgeranylation reaction
- MI:0994 demyristoylation assay -> MI:0201 demyristoylation reaction
- MI:0995 depalmitoylation assay -> MI:0202 depalmitoylation reaction

2) Interaction detection method and participant's biological role

a) Oxidoreductase assay (MI:0979)

Each participant's biological role **should** be one of the following terms :

- electron donor (MI:0579)
- electron acceptor (MI:0580)

b) Phosphotransfer assay (MI:0841)

Each participant's biological role **should** be one of the following terms :

- phosphate donor (MI:0842)
- phosphate acceptor (MI:0843)

c) Enzymatic study (MI:0415)

Each participant's biological role **should** be one of the following terms :

- enzyme (MI:0501)
- enzyme target (MI:0502)

d) Bioluminescence resonance energy transfer (MI:0012)

Each participant's biological role **should** be one of the following terms :

- donor (MI:0918)
- acceptor (MI:0919)

- unspecified role (MI:0499)

e) Fluorescent resonance energy transfer (MI:0055)

Each participant's biological role **should** be one of the following terms :

- donor (MI:0918)
- acceptor (MI:0919)
- unspecified role (MI:0499)

e) Homogeneous time resolved fluorescence (MI:0510)

Each participant's biological role **should** be one of the following terms :

- donor (MI:0918)
- acceptor (MI:0919)
- unspecified role (MI:0499)

3) Interaction detection method and participant's experimental role

*a) Interaction detection methods for which each participant's experimental role **should** be neutral component (MI:0497)*

- light scattering (MI:0067)
- nuclear magnetic resonance (MI:0077)
- Cross-linking study and its children (MI:0030)
- X-ray crystallography and its children (MI:0114)
- intermolecular force (MI:0859)
- small angle neutron scattering (MI:0888)
- neutron fiber diffraction (MI:0891)
- neutron diffraction (MI:0893)
- electron diffraction (MI:0894)
- amplified luminescent proximity homogeneous assay (MI:0905)
- rheology measurement (MI:0938)
- classical fluorescence spectroscopy (MI:0017)
- fluorescence correlation spectroscopy (MI:0052)
- fluorescence polarization spectroscopy (MI:0053)
- molecular sieving (MI:0071)
- detection by mass spectrometry and its children (MI:0943)
- cosedimentation and its children (MI:0027)
- filter trap assay (MI:0928)
- saturation binding (MI:0440)
- enzyme linked immunosorbent assay and its children (MI:0411)
- enzymatic study and its children (MI:0415)
- footprinting and its children (MI:0417)
- comigration in gel electrophoresis and its children (MI:0807)
- gdp/gtp exchange assay (MI:0949)
- polymerization (MI:0953)

- image technique and its children (MI:0428)

*b) Interaction detection methods for which each participant's experimental role **should** be either bait (MI:0496), prey (MI:0498) or unspecified role (MI:0499)*

- scintillation proximity assay (MI:0099)
- surface plasmon resonance (MI:0107)
- protein complementation assay and its children (MI:0090)
- affinity chromatography technology and its children (MI:0004)
- ion exchange chromatography (MI:0226)
- reverse phase chromatography (MI:0227)
- array technology (MI:0008)
- display technology and its children (MI:0034)

4) Interaction detection method and participant identification method

*a) Interaction detection methods for which each participant's identification method **should** be predetermined participant (MI:0396)*

- circular dichroism (MI:0016)
- electron resonance (MI:0043)
- isothermal titration calorimetry (MI:0065)
- light scattering (MI:0067)
- nuclear magnetic resonance (MI:0077)
- surface plasmon resonance and its children (MI:0107)
- x-ray crystallography and its children (MI:0114)
- intermolecular force (MI:0859)
- small angle neutron scattering (MI:0888)
- neutron fiber diffraction (MI:0891)
- neutron diffraction (MI:0893)
- electron diffraction (MI:0894)
- amplified luminescent proximity homogeneous assay (MI:0905)
- rheology measurement (MI:0938)
- light microscopy (MI:0426)
- x-ray tomography (MI:0827)
- atomic force microscopy (MI:0872)
- enzymatic study and its children (MI:0415)

b) Protein complementation assay and its children (MI:0090)

Each participant's identification method **should** be one of the following terms :

- predetermined participant (MI:0396)
- nucleotide sequence identification (MI:0078)

c) Electron microscopy (MI:0040)

Each participant's identification method **should** be one of the following terms :

- predetermined participant (MI:0396)
- immunostaining (MI:0422)

d) Fluorescence microscopy (MI:0416) and confocal microscopy (MI:0663)

Each participant's identification method **should** be one of the following terms :

- tag visualisation by fluorescence (MI:0867)
- immunostaining (MI:0422)

5) Database cross reference and reference qualifier

a) Experiment level

a.1) Pubmed (MI:0446) cross reference

The reference qualifier **must** be one of the following terms :

- primary-reference (MI:0358)
- see-also (MI:0361)
- method reference (MI:0357)
- source reference (MI:0685)

a.2) DOI (MI:0574) cross reference

The reference qualifier **must** be one of the following terms :

- primary-reference (MI:0358)
- see-also (MI:0361)

b) Interaction level

b.1) Pubmed (MI:0446) cross reference

The reference qualifier **must** be one of the following terms :

- see-also (MI:0361)

b.2) Gene ontology (MI:0448) cross reference

The reference qualifier **must** be one of the following terms :

- gene ontology for cellular component (MI:0354)
- gene ontology for cellular function (MI:0355)
- gene ontology for cellular process (MI:0359)

b.3) Wwpdb (MI:0805) cross reference

The reference qualifier **must** be one of the following terms :

- identical object (MI:0356)

c) Interactor level

c.1) Pubmed (MI:0446) cross reference

The reference qualifier **must** be one of the following terms :

- identical object (MI:0356)

d) Participant level

d.1) Uniprot knowledge base (MI:0486) cross reference

The reference qualifier **must** be one of the following terms :

- identical object (MI:0356)

d.2) Ref-seq (MI:0481) cross reference

The reference qualifier **must** be one of the following terms :

- identical object (MI:0356)
- secondary accession number (MI:0360)

e) Feature level

e.1) Interpro (MI:0449) cross reference

The reference qualifier **must** be one of the following terms :

- identical object (MI:0356)

6) Feature type and feature detection method

a) Binding sites (MI:0117) and its children

The feature detection method **should** be one of the following terms :

- full identification by DNA sequencing (MI:0056)
- mutation analysis or one of its children (MI:0074)
- X-ray cristallography or one of its children (MI:0114)
- western blot or one of its children (MI:0113)
- protein footprinting (MI:0436)

b) Mutations (MI:0118)

The feature detection method **should** be one of the following terms :

- mutation analysis (MI:0074)

7) Feature type and feature range status

a) Tags (MI:0507) and its children

The feature range status (start and end) **should** be one of the following terms :

- c-terminal range (MI:1039)
- n-terminal range (MI:1040)
- undetermined sequence position (MI:0339)

b) Isotope label (MI:0253) and its children

The feature range status (start and end) **should** be one of the following terms :

- undetermined sequence position (MI:0339)