The PhenX Toolkit - make data sharing easier

NIEHS Data Sharing Workshop

Carol M. Hamilton, PhD
February 6, 2012
PhenX: consensus measures for Phenotypes and eXposures

• In September 2007, RTI International was awarded (via a Cooperative Agreement with NHGRI) this project to select and define high priority measures for Genome-wide association studies (GWAS)

• NHGRI recognized that the development of standard measures for use in GWAS would have significant impact on biomedical research – and decided to address the problem

• The development of a PhenX Toolkit is envisioned as a way to facilitate broad use of these measures by the research community
Standard Measures Needed

• Multi-IC Symposia on Applying Genomics Technologies to Population Studies (2006)
  – Recommendations:
    • Limited subsets of phenotypic and exposure data that are amenable to common definition and standardized collection in GWAS should be identified in near future
    • Better methods for phenotyping (rigorous, standardized, inexpensive, non-invasive, limited burden, appropriate for asymptomatic individuals) are needed, particularly for phenotypes relevant to a wide variety of diseases and disabilities

  – Recommendations:
    • Identify a subgroup of phenotypes and exposures with strong genetic associations for standardization and addition to GWAS
    • Support the review of phenotype and exposure data deposited in dbGaP to identify the most common measures and those that can be used in multiple studies.
PhenX Approach

- The approach was to select 15 high-priority measures for each of 21 research domains
  - Domains were selected by the PhenX Steering Committee
  - Measures and protocols were chosen by Working Groups which are assembled for each domain
  - Scientific community had the opportunity to review and comment on initial set of up to 25 measures for each domain
- Selected measures are made available to the research community via the PhenX Toolkit to facilitate future cross-study analysis
- Initial phase was launched in October 2008; all 21 domains were in the Toolkit in December 2010
PhenX - Building Consensus

- PhenX Steering Committee (SC)
  - Provides guidance to the project
  - Selects domains and define scope

- NIH Institutes and Centers (IC) Liaisons to SC
  - Provide expertise, outreach

- Expert Working Groups assembled for each domain
  - Refine the scope
  - Select specific measures and protocols

- Outreach to Scientific Community
  - Obtain comments for consideration by the Working Groups
PhenX Definitions

• **DOMAIN**: Topical area with a unifying theme (organ system, complex disease, lifestyle factors, etc.)

• **MEASURE**: Broadly refers to a certain characteristic of, or relating to, a study subject that you are interested in capturing data on

• **PROTOCOL**: standard procedure recommended by a Working Group for investigators to collect and record a PhenX measure
PhenX Definitions

- **DOMAIN**: Topical area with a unifying theme (organ system, complex disease, lifestyle factors, etc.)

  Environmental Exposures

- **MEASURE**: Broadly refers to a certain characteristic of, or relating to, a study subject that you are interested in capturing data on

  Air Contaminants in the Home Environment

- **PROTOCOL**: Standard procedure recommended by a Working Group for investigators to collect and record a PhenX measure

  Atmospheric and Environmental Research (AER) Inc.
PhenX Domains

- Alcohol, Tobacco, and Other Substances
- Anthropometrics
- Cancer
- Cardiovascular
- Demographics
- Diabetes
- Environmental Exposures
- Gastrointestinal
- Infectious Diseases and Immunity
- Neurology
- Nutrition and Dietary Supplements
- Ocular
- Oral Health
- Physical Activity and Physical Fitness
- Psychiatric
- Psychosocial
- Reproductive Health
- Respiratory
- Skin, Bone, Muscle, and Joint
- Social Environments
- Speech and Hearing
Welcome to the PhenX Toolkit

The Toolkit provides standard measures related to complex diseases, phenotypic traits and environmental exposures. Use of PhenX measures facilitates combining data from a variety of studies, and makes it easy for investigators to expand a study design beyond the primary research focus.

Toolkit Users can:

- Search or Browse the Toolkit to review and select PhenX measures
- Generate Data Collection Worksheets and Data Dictionaries for Selected Measures

Information about the project is available at www.phenx.org

Please read Toolkit Guidance

Please cite use of the PhenX Toolkit:


Measures from the PhenX Toolkit version November 29 2011, Ver 4.6 (www.phenxtoolkit.org) were included in this study. PhenX (consensus measures of Phenotypes and eXposures) is supported by NHGRI award No. U01 HG004597.

PhenX Toolkit Release Notes

Please take a quick survey to tell us how we can improve the Toolkit.

There are a total of 295 measures in the PhenX Toolkit.

<table>
<thead>
<tr>
<th>Top 5 Measures - Release 4.6</th>
<th>Top 5 Domains - Release 4.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Current Age</td>
<td>1. Demographics</td>
</tr>
<tr>
<td>2. Gender</td>
<td>2. Anthropometrics</td>
</tr>
<tr>
<td>3. Ethnicity</td>
<td>3. Alcohol, Tobacco and Other Substances</td>
</tr>
<tr>
<td>4. Race</td>
<td>4. Cardiovascular</td>
</tr>
<tr>
<td>5. Weight</td>
<td>5. Environmental Exposures</td>
</tr>
</tbody>
</table>

View Top 20 Measures
PhenX Toolkit

• Researchers will visit the Toolkit to:
  – Add standard measures to ongoing studies
  – Consider PhenX measures when planning new studies
  – Obtain high quality measures outside of their area of expertise
  – Review PhenX measures that relate to their primary research focus

• By selecting some of the PhenX measures:
  – Ensure that their study will be compatible with others that also incorporate PhenX measures
  – Combine studies to increase statistical power and the ability to identify genes associated with complex diseases
  – Potential to cumulatively combine with future studies
Facilitating Cross-Study Analysis

- Select PhenX Measures from the Toolkit
- CVD
- Diabetes
- Obesity
- Future Studies

Combine Study Results
- Increased Sample Size + Increased Statistical Power

Detect More Subtle and/or More Complex Gene Associations
PhenX Toolkit Contents

- Recommended measures for each research domain
- Detailed protocols for collecting the measures
- Information about the measures
  - Rationale for inclusion
  - References
- User support
  - User’s Manual, Data Dictionary, and Glossary of Terms
  - Quick Start Guide
  - Frequently Asked Questions (FAQs)
  - Derived Variables
  - Cancer Bioinformatics Grid (caBIG) Common Data Elements (CDEs)
  - Supplemental Information
**Toolkit Features**

- **Users can Search or Browse Measures**
  - Browse by domain or collection
  - Search using “Smart Query Tool”
- **Users choose Measures and add them to “My Toolkit”**
  - Alerts Users to add “essential measures” (additional PhenX measures that are needed to effectively interpret the data)
  - Recommends related measures
  - Registration allows users to save and share multiple Toolkits
- **Users can generate Reports**
  - Download, review, print or save
  - Registered users can add notes to measures, and protocols
- **Integrating PhenX Measures**
  - Data Collection Worksheet
  - Data Dictionary (variable names and characteristics)
Browse Measures

Show Tree

Browse through Measures to view Protocols.

Browse » Domains »

**DOMAIN:** Environmental Exposures 060000

- Release Date: October 30, 2009
- View scope of domain
- View Supplemental Information
- View Working Group Roster

- Add to My Toolkit 061100 Air Contaminants in the Home Environment
- Add to My Toolkit 060100 Characteristics of Current Residence
- Add to My Toolkit 060700 Current Environmental Tobacco Smoke Exposure
- Add to My Toolkit 060900 Day Care/Preschool Attendance
- Add to My Toolkit 061000 History of Being Breast Fed
- Add to My Toolkit 060500 Occupation/Occupational History
- Add to My Toolkit 061400 Plastic Exposures at Work and Home
- Add to My Toolkit 060300 Residential History
Protocol Overview

Browse » Domains » Physical Activity and Physical Fitness » Cardiorespiratory Fitness - Exercise Test Estimate » Card [One Mile Walk]

Note: Some Protocols contain images. You may click the thumbnails to preview the full image. To print Protocols with full size images, please select a Report.

Cardiorespiratory Fitness-Exercise Test Estimate [One Mile Walk]  #150101

Protocol Release Date

May 12, 2010

Description of Protocol

The participant is asked to complete a one-mile walk test as quickly as possible on a track. A technician utilizes a stopwatch to rate monitor that records h/her heart rate continuously through the test. After the test is completed the technician records the test. In addition, the participant’s age, sex, and body weight are needed to complete an equation to determine maximal oxygen

Specific Instructions

Protocol Text

Track or pre-measured one-mile distance
Protocol Overview

Browse ➔ Domains ➔ Physical Activity and Physical Fitness ➔ Cardiorespiratory Fitness - Exercise Test Estimate ➔ Cardiorespiratory Fitness-Exercise Test Estimate [One Mile Walk]

Note: Some Protocols contain images. You may click the thumbnails to preview the full image. To print Protocols with full size images, please add those Protocols to your Toolkit and Generate a Report.

Cardiorespiratory Fitness-Exercise Test Estimate [One Mile Walk] "150101"

Jump to section: 
- Description of Protocol
- Special Instructions
- Protocol Text
- Protocol Release Date
- Selection Rationale
- Source
- Personnel and Training Required
- Equipment Needs
- Standards
- General References
- Protocol Type
- Derived Variables
- Requirements
- Track or pre-measured one-mile distance

Perform a one-mile walk test as quickly as possible on a track. A technician utilizes a stopwatch to time the walk. The participant wears a heart rate monitor and the heart rate is continuously monitored throughout the test. After the test is completed, the technician records the heart rate from the last 10 seconds of the test. Age, sex, and body weight are needed to complete an equation to determine maximal oxygen consumption (VO2max).
Searching the Toolkit

- There is some overlap between the 21 research domains.
- For example, not all “tobacco” related measures are in the ATOS domain; not all diabetes related measures are in the Diabetes domain.
- Each WGs reviewed the measures already in the Toolkit before proceeding, but this became more complicated as more domains were completed.
- The Search features of the Toolkit make it easy for users to find measures of interest from any domain in the Toolkit.
PhenX Smart Query Tool

- **Search with Filters**
  - Filter search results using protocol characteristics (Data Collection Mode, Lifestage, Time to Complete, and Language)

- **Smart Search**
  - Searches through measure names, aliases, and keywords; high specificity

- **Text Search**
  - Searches through full text of measures and protocols; high sensitivity

- **Supplemental Information**
  - Searchable in the full-text search only
Smart Query Tool

Search pre-defined search filters listed below
Search by entering your own terms in the box below

Data Collection Mode

<table>
<thead>
<tr>
<th>Lifestage</th>
<th>Time to Complete</th>
<th>Language</th>
</tr>
</thead>
</table>

Enter search term or PhenX ID:

Show 10 results per page

Smart Search  Text Search

Smart Search:
- Searches through names, aliases, and keywords; high-specificity
- Returns fewer results than the Text Search, but they are more specific

Text Search:
- Searches through full text of measures and protocols; high-sensitivity, low-specificity
- Returns more results than the Smart Search, but they are less specific
- Also searches through Supplemental Information

Helpful Search Tips:
- Use “quotation marks” to search for exact phrase
- For high specificity, search with a single key term. For example, to find “Family history of diabetes among first degree relatives”, search “family history” (with quotes)

See search logic for more details
Smart Query Tool

Enter search term or PhenX ID:

alcohol

Show 10 results per page

Smart Search  Text Search

Search with Filters: To filter results by the following parameters, please identify desired types of measures by clicking the filter name. The filters are: Data Collection Mode, Lifestage, Time to Complete and Language.

If no boxes are checked, then search results will reflect all Toolkit contents.

Data Collection Mode
- [ ] Interviewer-administered questionnaire
- [ ] Self-administered questionnaire
- [ ] Physical Measurement
- [ ] Bioassay
- [ ] Clinical Examination
- [ ] Medical records abstraction
- [ ] Secondary Data Analysis

Lifestage
- [ ] Infant
- [ ] Toddler
- [ ] Child
- [ ] Adolescent
- [ ] Adult
- [ ] Senior
- [ ] Pregnancy

Time to Complete
- [ ] <=15 minutes
- [ ] >15 minutes

Language
- [ ] English
- [ ] Spanish
- [ ] Other

9 search results in terms and synonyms for “alcohol”, 0 supplemental (27 filtered hide filters):

Search result 1 - 9 of 9 results

<table>
<thead>
<tr>
<th>PhenX Measure</th>
<th>Definition</th>
<th>Domain/Collection Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] Expectancies - Alcohol, Tobacco, and Other Substances</td>
<td>Instruments used separately to assess expectations of the positive and negative effects of drinking alcohol, smoking cigarettes, using marijuana, using illegal stimulant drugs, or misusing prescription stimulant drugs.</td>
<td>Substance-specific Intermediate Phenotypes</td>
</tr>
<tr>
<td>[ ] Alcohol - 30-Day Quantity and Frequency</td>
<td>Questions asking the respondent about quantity and frequency of alcohol consumption during the past 30 days.</td>
<td>Alcohol, Tobacco and Other Substances</td>
</tr>
</tbody>
</table>
Smart Query Tool

Enter search term or PhenX ID:

alcohol

Show [ ] results per page

Smart Search  Text Search

Search with Filters: To filter results by the following parameters, please identify desired types of measures by clicking the filter name.
The filters are: Data Collection Mode, Lifestage, Time to Complete and Language.
If no boxes are checked, then search results will reflect all Toolkit contents.

Data Collection Mode  Lifestage  Time to Complete  Language

36 search results in terms and synonyms for "alcohol", 0 supplemental (0 filtered - view filters):

Search result 1 - 10 of 36 results

- PhenX Measure  Definition  Domain/Collection Name
  - Expectancies - Alcohol, Tobacco, and Other Substances
    - Instruments used separately to assess expectations of the positive and negative effects of drinking alcohol, smoking cigarettes, using marijuana, using illegal stimulant drugs, or misusing prescription stimulant drugs.
    - Intermediate Phenotypes
  - Cumulative Lifetime Alcohol Exposure
    - Measure to determine total lifetime alcohol use
    - Cancer
  - Motives - Alcohol, Tobacco, and Other Substances
    - Instruments used separately to assess the motives (reasons) for drinking alcohol, smoking cigarettes, or using drugs.
    - Intermediate Phenotypes
  - Perceived Availability of Illegal Drugs and Alcohol
    - Instrument used to gather respondents' perceptions of the availability of substances including illegal drugs and alcohol.
    - Community Factors
  - Unmet Need for Alcohol or Drug Treatment
    - A measure of the treatment needs, service utilizations, and barriers of alcohol and drug treatment, based on data from the National Survey on Drug Use and Health (NSDUH).
    - Community Factors
Statistics-Based Recommendations
Data Sharing and Data Interoperability

Collaborations:

• National Library of Medicine (NLM)
  – National Center for Biotechnology Information (NCBI) database of Genotypes and Phenotypes (dbGaP)
  – Logical Observation Identifiers Names and Codes (LOINC)

• Cancer Data Standards Registry and Repository (caDSR) Common Data Element (CDE) at cancer Biomedical Informatics Grid (caBIG)

• electronic Medical Records & Genomics (eMERGE) network

• Public Population Project in Genomics (P3G) Data Schema and Harmonization Platform for Epidemiological Research (DataSHaPER)
Collaboration with dbGaP

- Highlight PhenX measure for variables in dbGaP

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>Dataset</th>
<th>Variable Description</th>
<th>Variable ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBP SBHS</td>
<td>dbGaP:021:2 trans</td>
<td>HIGH BLOOD PRESSURE: Subject History of disease</td>
<td>ph00081405.v1.p1</td>
</tr>
<tr>
<td>HBP FAMHS</td>
<td>dbGaP:021:2 trans</td>
<td>HIGH BLOOD PRESSURE: Family History of disease</td>
<td>ph00081406.v1.p1</td>
</tr>
<tr>
<td>HBP FAMNO</td>
<td>dbGaP:021:2 trans</td>
<td>HIGH BLOOD PRESSURE: Number of family members with history of disease</td>
<td>ph00081407.v1.p1</td>
</tr>
<tr>
<td>HBP SBHS</td>
<td>dbGaP:041:1 trans</td>
<td>HIGH BLOOD PRESSURE: Subject History of disease</td>
<td>ph00081538.v1.p1</td>
</tr>
<tr>
<td>HBP FAMHS</td>
<td>dbGaP:041:1 trans</td>
<td>HIGH BLOOD PRESSURE: Family History of disease</td>
<td>ph00081537.v1.p1</td>
</tr>
<tr>
<td>HBP FAMNO</td>
<td>dbGaP:041:1 trans</td>
<td>HIGH BLOOD PRESSURE: Number of family members with history of disease</td>
<td>ph00081538.v1.p1</td>
</tr>
<tr>
<td>HBP SBHS</td>
<td>dbGaP:041:1 trans</td>
<td>HIGH BLOOD PRESSURE: Subject History of disease</td>
<td>ph00081683.v1.p1</td>
</tr>
<tr>
<td>HBP FAMHS</td>
<td>dbGaP:041:1 trans</td>
<td>HIGH BLOOD PRESSURE: Family history of disease</td>
<td>ph00081684.v1.p1</td>
</tr>
<tr>
<td>HBP FAMNO</td>
<td>dbGaP:041:1 trans</td>
<td>HIGH BLOOD PRESSURE: Number of family members with history of disease</td>
<td>ph00081685.v1.p1</td>
</tr>
<tr>
<td>BPD</td>
<td>dbGaP:041:1 trans</td>
<td>Diastolic Blood Pressure</td>
<td>ph00082600.v1.p1</td>
</tr>
<tr>
<td>BPS</td>
<td>dbGaP:041:1 trans</td>
<td>Systolic Blood Pressure</td>
<td>ph00082600.v1.p1</td>
</tr>
</tbody>
</table>

Variable mapped to PhenX measure can be flagged
Toolkit Use Summary
(www.phenxtoolkit.org December 2011)

Number of Visits: 259,077
Number of Unique Visits: 52,992
(by unique IP address)
Total Page Views: 1,072,785
Average Number Visits Per Day: 223
Total # of Countries with Toolkit Accesses: 146
Number of Registered Users: 696
Visits from the United States
PhenX – more

• NIDA is currently sponsoring a one year Administrative Supplement to expand the Toolkit to support NIDA research
  – Envision product as one “Core” collection of measures and six “Specialty” collections of measures
  – Core measures would be suitable for all NIDA investigators, Specialty measures would be included as appropriate

• NHGRI – OBRRS Administrative Supplement to incorporate PhenX measures (for NIH funded projects)
  – PhenX RISING, Real World Implementation, and SharING
Substance Abuse and Addiction (SAA) Collections
- coming soon, Feb 24

• Core Collections
  – Core: Tier 1
  – Core: Tier 2

• Specialty Collection
  – 1. Assessment of Substance Use and Substance Use Disorders
  – 2. Substance-specific Intermediate Phenotypes
  – 3. Substance Use-related Neurobehavioral and Cognitive Risk Factors
  – 4. Substance Use-related Psychosocial Risk Factors
  – 5. Substance Use-related Community Factors
  – 6. Substance Use-related Co-morbidities and Health-related Outcomes
Presenting SAA measures in the Toolkit

Welcome to the PhenX Toolkit

The Toolkit provides standard measures related to complex diseases, phenotypic traits and environmental exposures. Use of PhenX measures facilitates combining data from a variety of studies, and makes it easy for Investigators to expand a study design beyond the primary research focus.

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More »

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Please cite use of the PhenX Toolkit:


Measures from the PhenX Toolkit version July 29 2011, Ver 4.5 (www.phenxtoolkit.org) were included in this study. PhenX (consensus measures of Phenotypes and eXposures) is supported by NIHGRI award No. U01 HG004597.
<table>
<thead>
<tr>
<th>PI/Institution</th>
<th>Study Name</th>
<th>NIH IC</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allison Aiello, Ph.D., University of Michigan</td>
<td>Ecologic Stressors, Post-Traumatic Stress Disorder, and Drug Use in Detroit</td>
<td>NIDA</td>
<td>PTSD co-morbidities; illicit drug use and coronary artery disease</td>
</tr>
<tr>
<td>Robert Bilder, Ph.D., UCLA</td>
<td>Human Translational Applications Core</td>
<td>NIMH</td>
<td>Neuropsychiatric and cognitive phenotypes</td>
</tr>
<tr>
<td>Terry Jernigan, Ph.D., UCSD</td>
<td>Creating a Pediatric Imaging-Genomics Data Resource</td>
<td>NIDA</td>
<td>Young adult risk and substance abuse behaviors; public pediatric imaging genomics db</td>
</tr>
<tr>
<td>Catherine McCarty, Ph.D., Essentia Institute of Rural Health</td>
<td>Genome-Wide Study of Cataract and Low HDL in Personalized Medicine Research Project</td>
<td>NHGRI</td>
<td>Cataract and HDL levels</td>
</tr>
<tr>
<td>Dharambir Sanghera, Ph.D., University of Oklahoma</td>
<td>Genome-Wide Association Scan to Identify Risk Genes for Type 2 Diabetes in Asian Indians</td>
<td>NIDDK</td>
<td>Type 2 diabetes and cardiovascular disease complications</td>
</tr>
<tr>
<td>Timothy Strauman, Ph.D., and Ahmad Hariri, Ph.D., Duke University</td>
<td>Self-Regulation Failure: Identifying and Modifying a Risk Phenotype</td>
<td>NIDA</td>
<td>Environmental influences on genes, brains, and behavior. Also includes MRI imaging</td>
</tr>
<tr>
<td>Zeng Yi, Ph.D., Duke University</td>
<td>Determinants of Healthy Longevity in China</td>
<td>NIA</td>
<td>Health and survival at old ages</td>
</tr>
</tbody>
</table>
PhenX Measures – Early Adopters

- NEIGHBOR Consortium (NEI funded)
- Gulf Long-Term Follow-up Study (GuLF STUDY) (NIEHS funded)
- Children’s Health after the Storm (CHATS) (CDC funded)
- Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) (NINDS funded)
- North American Pancreatitis Study 2 Continuation and Validation (NAPS2-CV) (NIDDK funded)
- GARM II: A Study on the Genetics of Age-related Maculopathy (NEI funded)
Measuring Exposures

EVERY BITE YOU TAKE

high-tech gadgets to measure the human ‘exposome’

Brandon Borrell,
Nature Vol 270, 17 Feb 2011

Medical devices

Inhaling information
How to collect data on asthma while, at the same time, treating it

IN 1985 and 1986 an epidemic of asthma hit Barcelona. The city’s researchers first turned to the usual suspects, such as air pollution, pollen and mould. But a series of telephone interviews with the sufferers pointed to a much more precise cause. All the attacks had occurred by the harbour, and at times when ships were unloading soya beans. The cause was clear: soya-bean dust. So was the solution: the installation of filters on the harbour’s silos.

Asthma is one of the world’s most common chronic diseases. It affects about 300m people (almost 5% of the population). Yet what triggers any given asthma attack is often unclear and, as a consequence, most asthmatics are not properly treated.

Stories of success, like that of Barcelona...
Resources

• **www.phenx.org**
  – Register to receive periodic updates via e-mail of the PhenX Newsletter and notification of new surveys

• **www.phenxtoolkit.org**
  – Additional measures and protocols will be included in the toolkit as they become available

• **www.genome.gov/gwastudies/**
  – A catalog of published Genome-Wide Association Studies (Hindorff et al. PNAS 2009)
Acknowledgements

- NHGRI
  - Erin Ramos (Project Scientist)
  - Heather Junkins (Project Analyst)
  - Teri Manolio
- SC Members (12)
  - Jonathan Haines, Chair
  - Bill Harlan, Vice-Chair
- WG Chairs / Members
- SSP (Advisory Panel for NIDA funded Substance Abuse and Addiction Supplement)
- IC Liaisons
- dbGaP
  - Kim Tryka
  - Jayashri Mehta
  - Steve Sherry
- LOINC
  - Clem McDonald
  - Daniel Vreeman
- P3G
  - Isabel Fortier
  - Paul Burton
- eMERGE
  - Rex Chisolm, Chris Chute, Dan Masys, Cathy McCarthy

- RTI Team
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  - Dean Jackman
  - Richard Kwok (NIEHS)
  - Debbie Maiese
  - Destiney Nettles
  - Helen Pan
  - WG Managers
  - Toolkit team
  - XC team
  - Communications team
  - Logistics team