Bay Area
useR Group
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Building **Trust** in Open Source Scientific Software

Grassroots Software Validation for R

Doug Kelkhoff
Sr Data Analyst
Genentech/Roche

R Validation Hub
PSI EFSPI R consortium

phuse

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Who am I

- Eager to improve **reproducibility** and **transparency** in Pharma
- Vested in enabling best possible decisions for therapeutics
- Believe in the collective power of groups with shared vision
- Contributing to **containerized analysis** pilots with FDA (PhUSE Data Visualization Workstream*)
- Contributing toward the **R Validation Hub** project under the R Consortium (www.pharmar.org)

*PhUSE Best Practices for Interactive Analsysis for Decision Making Workstream

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What I Do

1 Scientists discover promising theraputic

2 Viable manufacturing research

3 Clinical trial run

4 Analysis to prove efficacy, safety

Health Authority (HA) reviews analysis 5

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What I Do

4 Analysis to prove efficacy, safety

- Extremely time-sensitive
- High throughput, predominantly heavily standardized analysis
- Emphasis on consistency, reliability
- Increasing requests for novel analysis
  (Most easily performed using open source tooling)
- Constant drive to expedite delivery of analysis to Health Authorities

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What We Need

4 Analysis to prove efficacy, safety

- Extremely time-sensitive — ***speed***
- High throughput, predominantly heavily standardized analysis — ***reproducibility***
- Emphasis on consistency, reliability
- Increasing requests for novel analysis — ***flexibility***
  (Most easily performed using open source tooling)
- Constant drive to expedite delivery of analysis to Health Authorities — ***transparency***

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Validating Clinical Software

a brief history

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Validating Clinical Software

Requirements

- Trustworthy
- Reliable
- Auditable

  "Generally equivalent to paper records"

[1] CFR Title 21 (1997)
[2] R Validation Hub Validation White Paper (2020)

Validating Clinical Software

Requirements	**Off-the-Shelf Analytic Software**
• Trustworthy	"Industry standard" "Accepted"
• Reliable	1 software version number
• Auditable "Generally equivalent to paper records"	Years of corporate process built around established tools

[1] CFR Title 21 (1997)
[2] R Validation Hub Validation White Paper (2020)

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Validating Clinical Software

Requirements	**Open Source Software**
• Trustworthy	"Some random code from the internet"
• Reliable	1000s of interrelated package versions
• Auditable "Generally equivalent to paper records"	Completely new territory for proving installation reproducibility

[1] CFR Title 21 (1997)
[2] R Validation Hub Validation White Paper (2020)

Validating Clinical Software

in an open-source driven world

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Validating R

1. **Documenting**
   a decision-making process that leads us to trust R packages

2. **Reproducibly Installing**
   R and packages

Validating R

1. **Documenting**
   a decision-making process that leads us to trust R packages

2. **Reproducibly Installing**
   R and packages

{riskmetric}

Containerized Analysis Pilot

[1] github.com/pharmaR/riskmetric
[2] PhUSE Interactive Analytics Working Group

Validating R

{riskmetric}

Analysis Packages
dplyr
limma
nlme
cowsay
shiny
beepr

pharmaR/riskmetric

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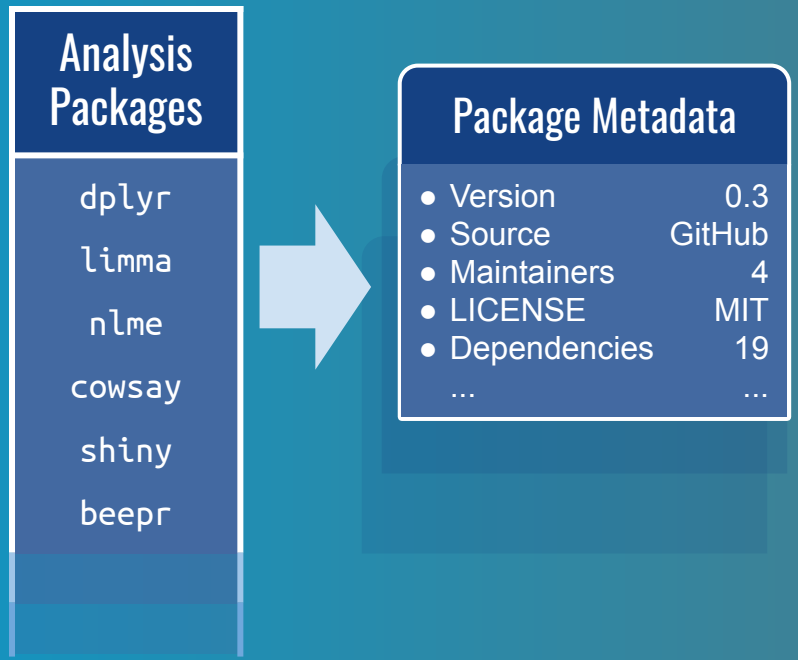
Validating R

{riskmetric}



pharmaR/riskmetric

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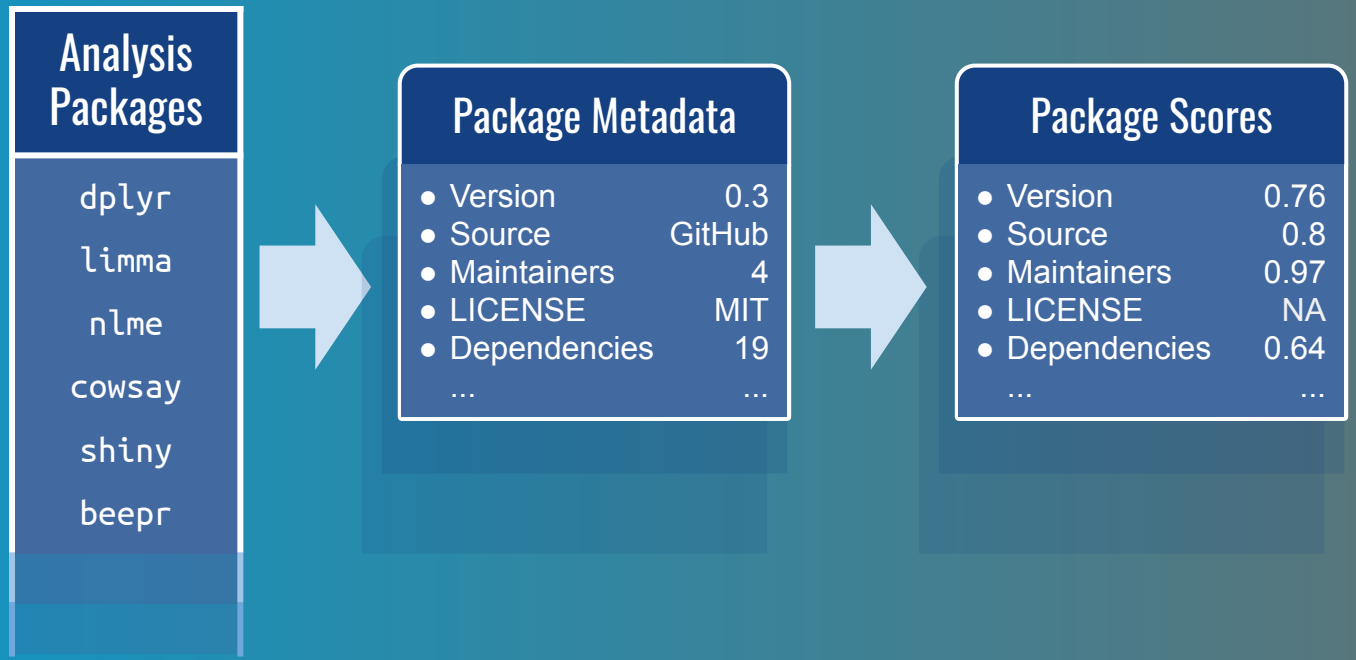
Validating R

{riskmetric}



pharmaR/riskmetric

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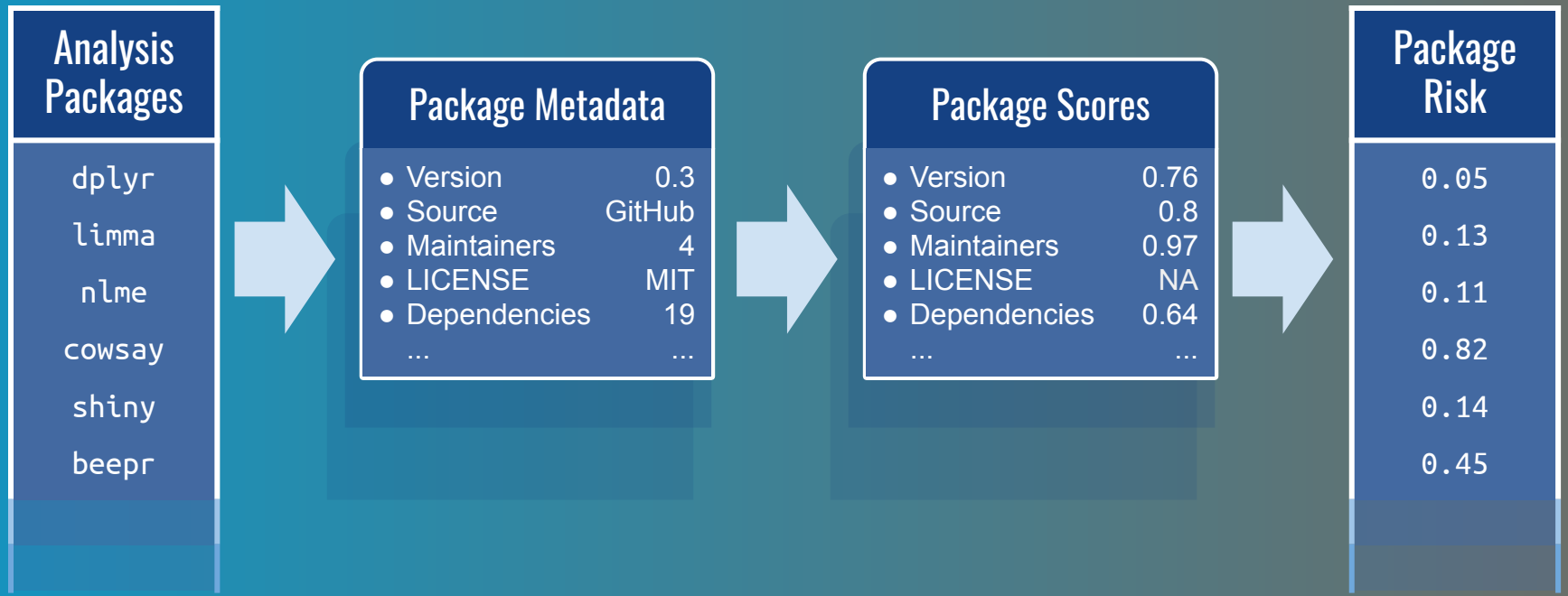
Validating R

{riskmetric}



pharmaR/riskmetric

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Validating R

{riskmetric}

```
library(riskmetric); library(tidyverse)

pkgs <- pkg_ref(c(
  "dplyr", "limma",
  "nlme"))

as_tibble(pkgs)
```

```
# A tibble: 3 x 3
  package version pkg_ref
  <chr>   <chr>   <list<pkg_ref>>
1 dplyr   0.8.4   dplyr<install>
2 limma   3.42.2  limma<bioc_remote>
3 nlme    3.1.141 nlme<install>
```

Validating R

{riskmetric}

```
library(riskmetric); library(tidyverse)

pkgs <- pkg_ref(c(
  "dplyr", "limma",
  "nlme"))

as_tibble(pkgs) %>%
  assess()
```

```
# A tibble: 3 x 10
  package version pkg_ref                 downloads_1yr
  <chr>   <chr>   <list<pkg_ref>>         <list<pkg_me>
1 dplyr   0.8.4   dplyr<install>          11654072
2 limma   3.42.2  limma<bioc_remote>      3611
3 nlme    3.1.141 nlme<install>           1267516
# … with 6 more variables:
```

Validating R

{riskmetric}

```
library(riskmetric); library(tidyverse)

pkgs <- pkg_ref(c(
  "dplyr", "limma",
  "nlme"))

as_tibble(pkgs) %>%
  assess() %>%
  score()
```

```
# A tibble: 3 x 10
  package version pkg_ref                 downloads_1yr
  <chr>   <chr>   <list<pkg_ref>>                   <dbl>
1 dplyr   0.8.4   dplyr<install>                   0.987
2 limma   3.42.2  limma<bioc_remote>              0.0235
3 nlme    3.1.141 nlme<install>                   0.894
# … with 6 more variables: license <dbl>,
```

Validating R

{riskmetric}

```
library(riskmetric); library(tidyverse)

pkgs <- pkg_ref(c(
  "dplyr", "limma",
  "nlme"))

as_tibble(pkgs) %>%
  assess() %>%
  score() %>%
  summarize_risk()
```

```
dplyr limma  nlme
  0.0   0.6   0.6
```

Validating R

{riskmetric}

Done

- # Downloads
- LICENSE
- # Open Repo Issues
- NEWS file
- ?help Documentation
- Vignettes

Planned

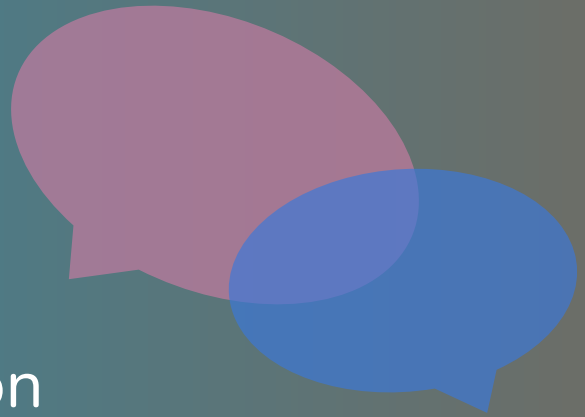
- Has maintainer
- Function Examples
- Param Docs
- Public Source Code
- Bug Responsiveness
- Statistical Standards
- # Active Contributors
- Code coverage
- Dependency coverage
- Patch Responsiveness
- Cyclomatic Complexity

Validating R

{riskmetric}

Contributions Welcome!

- Share your use case
- Help us spec out risk metrics
- Review vignettes / documentation
- Contribute code



Validating R

phuse Containerized Analysis Pilot

my analysis

FDA review

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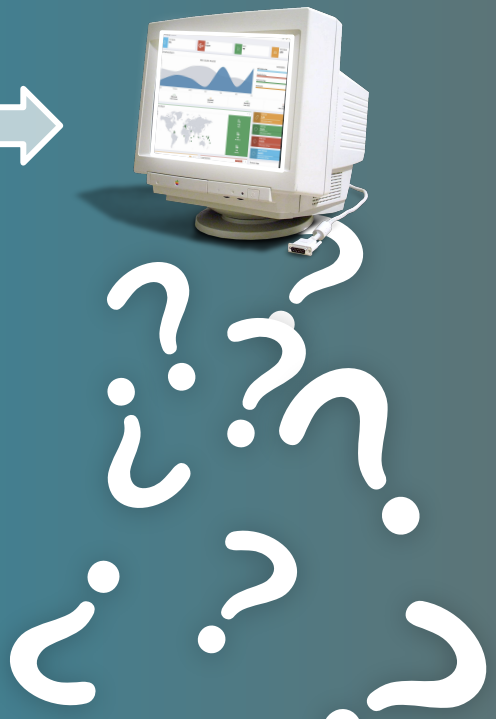
FDA review



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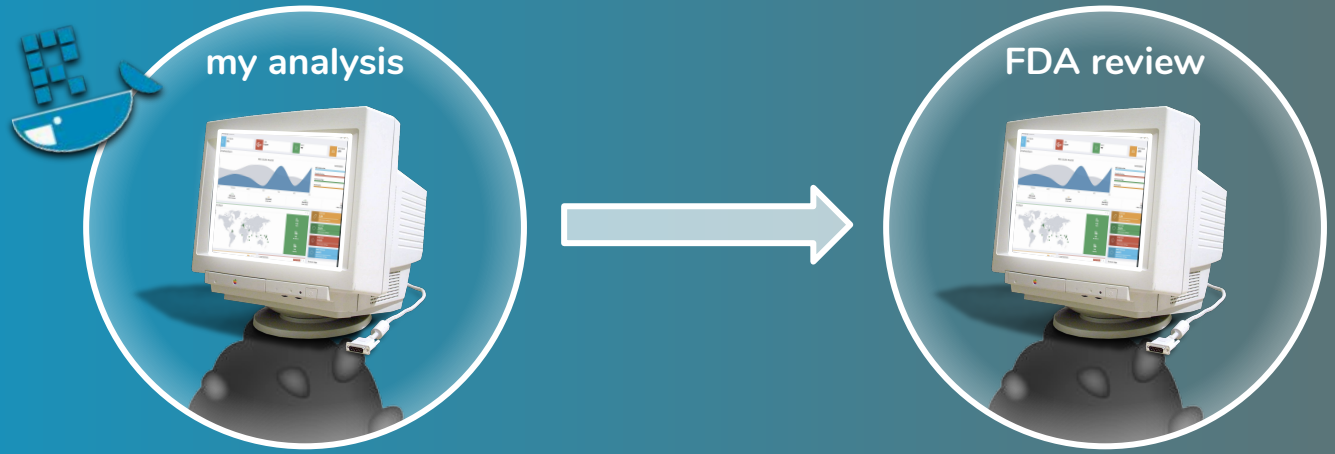
phuse Containerized Analysis Pilot



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Validating R

phuse Containerized Analysis Pilot + {riskmetric}


```
> library(riskmetric)
> report_risk(library_pkg_refs())
✓ haven v1.2.3   risk: 0.0032
✓ dplyr v0.8.3   risk: 0.0050
Writing risk assessment reports
to ~/.riskmetric/logs.
```

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Open Scientific Rigor

- Forming group to pilot testing framework for implementations of standardized methods
- Building upon rocker to support modular R containers
- “Modernization of Analytics” will also be focusing on risk assessment

TransCelerate BIOPHARMA INC.

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Putting it all together

Flexible, isolated internal analysis

Tools for adding context to “Trust”

Reliably reproducible results with “paper-equivalent” records

Added consistency throughout the industry


```
> library(riskmetric)
> report_risk(library_pkg_refs())

✓ haven v1.2.3
✓ dplyr v0.8.3
Writing risk assessment reports
to ~/.riskmetric/logs.
```

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Thanks / Q&A

Andy Nichols
Yilong Zhang
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Eric Nantz

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Nilesh Narayan
Paul Schuette
Alan Shapiro

Reinhold Koch
Craig Gower