Top 10 Regulatory Surveillance Signals of Summer 2022

Winter for you
Southern Hemisphere folks

Your Panelists

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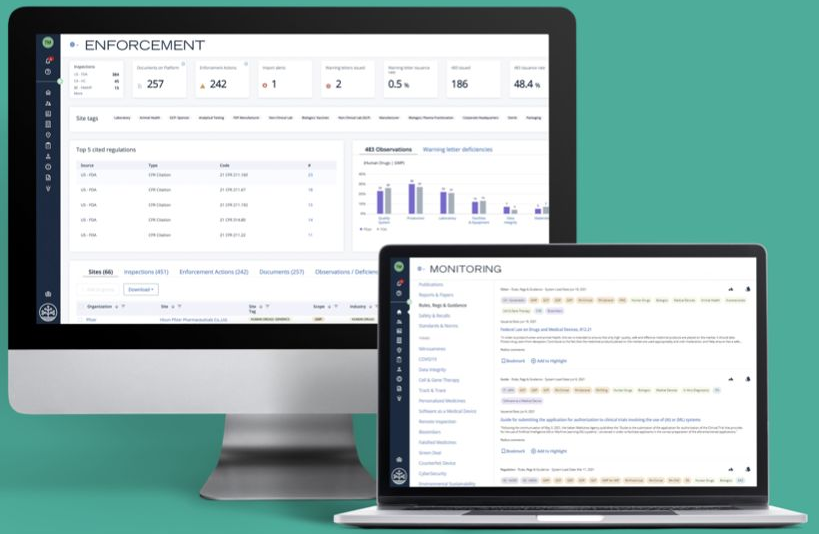
About Redica Systems

Redica Systems is a data analytics platform helping life sciences companies improve quality and stay on top of evolving regulations.



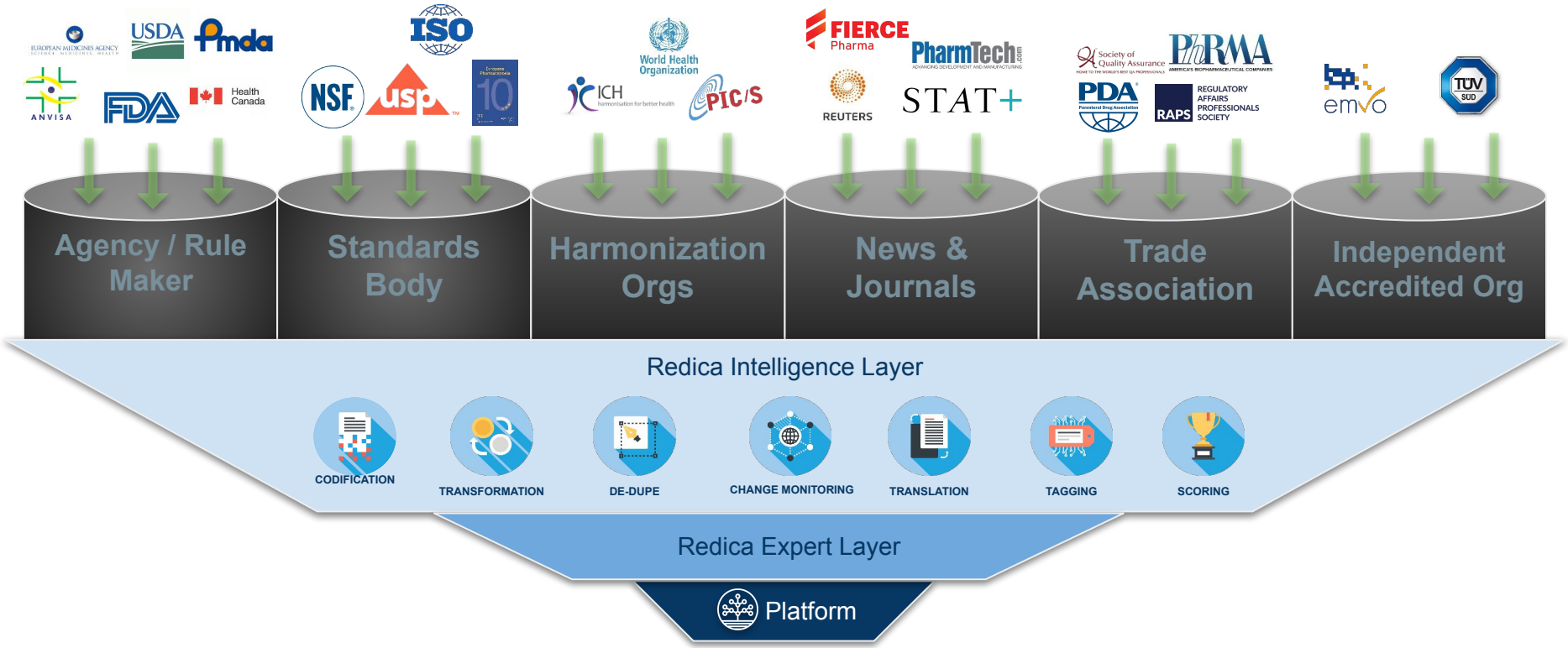
Who We Serve

We serve quality, safety, and supply chain management professionals at companies in regulated industries, like pharma, biopharma, medtech, medical device, and food and cosmetics industries.

Redica Systems serves over 200 customers in the pharma, medical devices and food industries, including 19 of the top 20 pharma companies and 9 of the 10 top medical devices companies.

External Monitoring

Module Data Overview: 15,000+ Curated URL Sources



Scope of our “Summer” retrospective

Industries

Human Drugs
& Biologics

+

Scopes

GMP
GDP
(HSE)
(Pharmacopeia)
(RA-CMC)

25 June to 29 August 2022

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Top Sources

- United States (US)
- European Union (EU)
- United Kingdom (GB)
- China (CN)
- Japan (JP)
- Canada (CA)
- Brazil (BR)
- Multinational
  ICH, PIC/S, WHO
- The EU Member states
- Russia
- EAEU/EEC
- India
- Korea
- Turkey
- Mexico
- Australia
- Saudi Arabia

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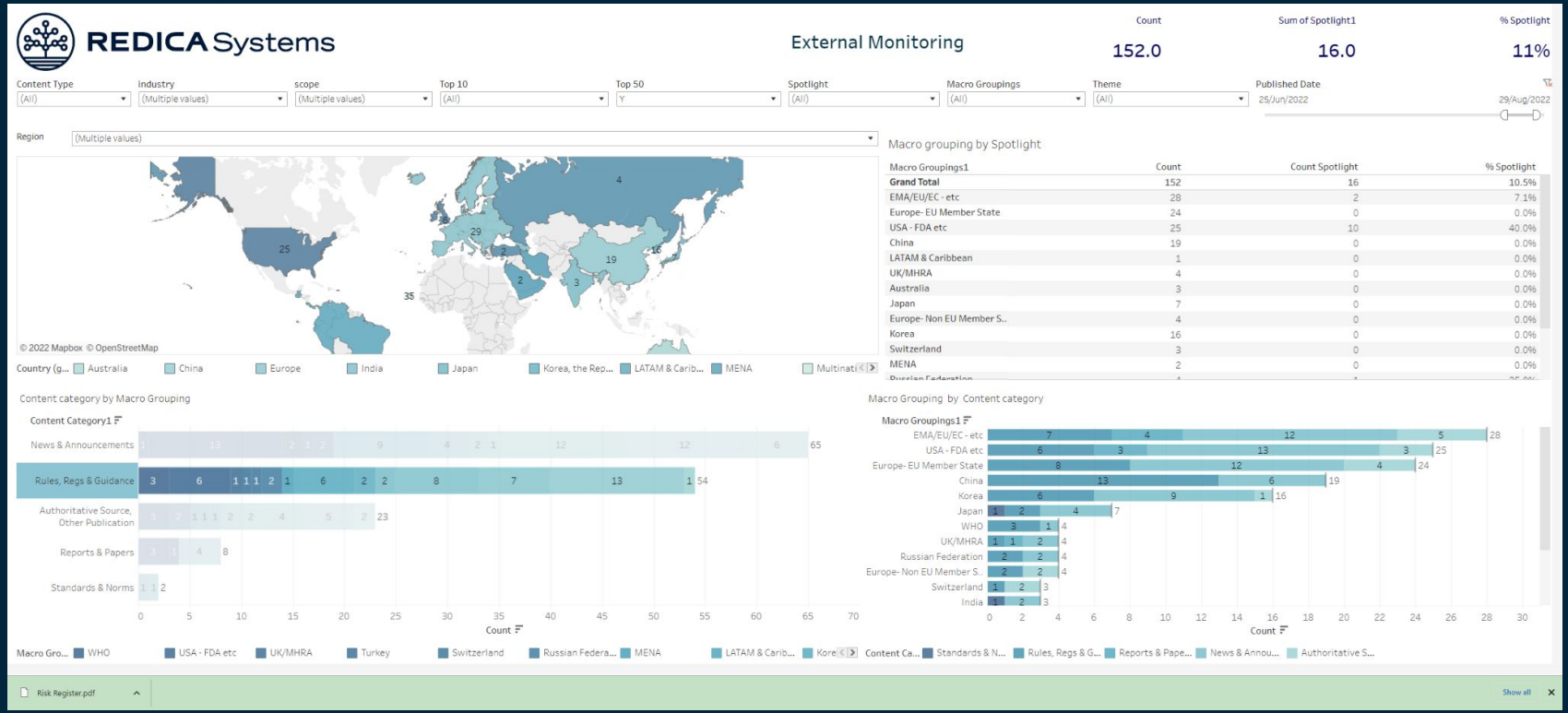
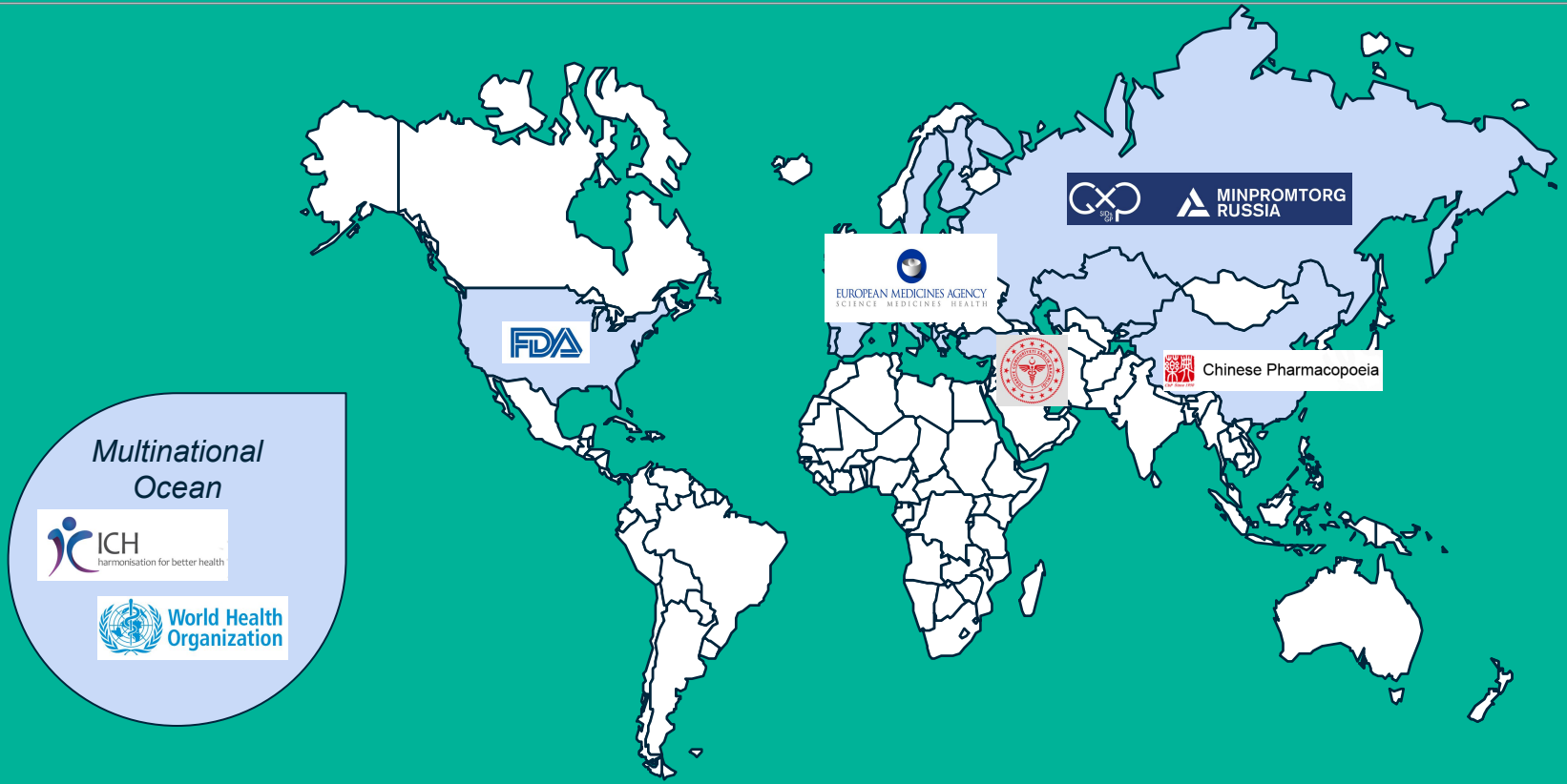
Top Content

- Rules, Regs and Guidance
- Authoritative Source, Other Publication
- Reports & Papers
- Standards & Norms

Our Signals at a glance



Our Top 10 Signals global footprint



EU GMP Annex 1 - An Evolution, and a Revolution

At long last, the EMA finalized and published the revised GMP Annex 1, the first complete revision since it was published originally in 1989:

- 4 ½ year wait to get to this point from the first draft issued in 2017, with >12 draft iterations
- a global effort with input from PICS and WHO to ensure consistency among the global requirements
- from 15 pages to 59 pages!
- primary product type = sterile drug products, however principles may be applied to non-sterile drug products manufacturing
- need for a Contamination Control Strategy (CCS) to be developed, implemented, and periodically reviewed
- existing sections expanded in detail and granularity
- new sections to address utilities, environmental monitoring process monitoring
- glossary added

Annex 1 of The Rules Governing Medicinal Products in the European Union Volume 4

FDA GMP framework for preventing cross-contamination - non-penicillin beta-lactam drugs manufacturing

A long awaited revision to the 2013 draft guidance:

- from 7 pages to 18 pages
- complete and comprehensive separation of the manufacturing operations of non-penicillin beta-lactam antibacterial drugs from the manufacturing operations of other drugs
- all compounds, including intermediates or derivatives, that are not a penicillin, have a chemical structure that includes one or more beta-lactam rings, and have a mechanism of action other than antibacterial mechanism of action
- recommendations for manufacturers of non-antibacterial beta-lactam compounds
- includes outsourcing facilities
- substantial glossary not included in the first
- FDA's interpretation of terms, such as allergic reaction, cross-reactivity
- distinction between non-penicillin beta-lactam antibacterial drug(s) and non-antibacterial beta-lactam compound(s)
- recommendations for drug manufacturers that seek to justify alternative cross-contamination prevention strategies for non-antibacterial beta-lactam compounds.

Non-Penicillin Beta-Lactam Drugs: A cGMP Framework for Preventing Cross-Contamination

China Pharmacopoeia GMP requirements' tsunami

Chinese Pharmacopoeia

China Pharmacopoeia Committee (CPC) published not less than 64 documents!

- applicable to the GMP area
- a range of content types: Rules, Standards, Guidelines, Analytical Methods, Explanatory notes, and Lists of proposed improvements
- a variety of topics such as pharmaceutical packaging materials, excipients, residual solvents, gas moisture determination etc
- an excellent opportunity for manufacturers to comment on the CPC's plan and anticipate requirements for implementation and enforcement.

Draft for comments on the general rules of rubber seals for pharmaceutical packaging ...and all other family members!

Russia/EAEU Data Integrity & CSV Guidance - GXP

Coming on the heels of International Regulators, Russia and the Eurasian Economic Area are positioning their Data Integrity and Computer Systems Validation requirements:

- organization of production and quality control of medicines for medical use AND veterinary use
- all records generated, maintained, and/or stored manually or electronically, from creation to archiving, to support the GMP processes used by pharmaceutical companies to ensure the high quality of their products from batch to batch
- all computerized systems that can have an impact on GMP
- guidance can be voluntarily used in other areas of Good Practice (GXP): distribution, clinical, laboratory and Good pharmacoVigilance Practices, as well as in other related areas – for example, in the activities of laboratories for quality control of medicines

Data Integrity and Validation of Computerized Systems

EMA Concept Paper - More to come for the ‘Management of Impurities’

EMA concept paper addresses the need to review and update the guideline on the chemistry of active substances:

- recognised as a need in the report on “Lessons learnt from presence of N-Nitrosamine impurities in sartan medicines”
- recommendations to reduce the risk of N-Nitrosamines being present in human medicines and to help the European medicines regulatory network be better prepared to manage future cases of unexpected impurities
- while in the last few years, experience has predominantly been gained in the management and risk mitigation of N-Nitrosamines, it is foreseen that (some of) the principles covered in revised guideline will apply to other Cohort of Concern (CoC) impurities and also other potent toxins.

Concept paper on the revision of the guideline on the chemistry of active substances

WHO Regulation Landscape - Advanced Therapy Products

This is WHO's current thinking on the regulation of Cell and Gene Therapy products, to promote convergence, and encourage the Member States to strengthen their regulatory system on both Human Cells and Tissues (HCTs) and Advanced Therapy Medicinal Products (ATMPs):

- not intended to be a comprehensive overview of regulatory requirements for either HCTs or ATMPs or the different regulatory frameworks that currently exist in different jurisdictions
- but, some of the fundamental principles that are important for providing adequate regulatory oversight for different types of cell and gene therapy products
- in the future, WHO will provide a more comprehensive overview and guidance on specific topics relevant to regulation of HCTs and ATMPs.

WHO approach towards the development of a global regulatory framework for Cell and Gene Therapy products

The EU Titanium Dioxide “Saga” - Further developments

Worth highlighting some further developments in this area with an updated Questions & Answers from EMA:

- five new questions and answers were added regarding replacement and removal of titanium dioxide in medicines for human and veterinary use (pages 15 to 20)
    - What does Commission Regulation (EU) 2022/63 on TiO2 mean
    - What to do as applicant of a Marketing Authorization Application (MAA)
    - What to do as Marketing Authorization Holder (MAH) of a Marketing Authorization (MA) containing TiO2
    - What are the scientific data requirements to remove/replace TiO2
    - What are the regulatory pathways to support a change in excipients to remove/replace TiO2 in medicinal products
- worksharing and collaboration among Marketing Authorization Holders (MAH) and National Competent Authorities (NCA) are encouraged

Replacement/removal of titanium dioxide (TiO2) in medicines

Turkey has a say in the GDP area

Let’s not underestimate Turkey on the side of influential Regulators.
Turkey issued in August its “Good Distribution Practices (GDP) Guidelines for Medicinal Products for Human Use”:

- procedures and principles regarding the purchase, sale, export, storage, distribution and shipment of medicinal products for human use
- in accordance with Good Distribution Practice (GDP) and relevant national and internationally accepted standards
- control & compliance of the supply chain to preserve the quality and integrity of products

Good Distribution Practices (GDP) Guidelines for Medicinal Products for Human Use

The new normal - Remote evaluations, assessments, reviews...

An achievement in the remote evaluation/remote inspection space as FDA has been striving to adapt to the new normal for more than 2 years and finally, issued this draft guidance on “Conducting Remote Regulatory Assessments (RRAs) Questions and Answers”:

- RRA to describe a category of activities for which FDA may use different terminologies, but that are all considered to be types of RRAs, including “remote interactive evaluations”, and “remote record reviews”
- RRA as an oversight of regulated industry while mitigating the spread of COVID-19 during the pandemic
- RRA becoming part of the new normal

Conducting Remote Regulatory Assessments Questions and Answers

ICH Q2/Q14 Consultation Lifecycle - One more follower

Following other Regulators, FDA issued its drafts for consultation on ICH Q2(R2) and ICH Q14. Comments were opened 26 August 2022 and closed 28 September 2022.

Public consultation dates Step 2b (from the ICH page)

ANVISA, Brazil - Deadline for comments by 31 August 2022

EC, Europe - Deadline for comments by 31 July 2022

FDA, United States - Deadline for comments by 28 September 2022

Health Canada, Canada - Deadline for comments by 13 September 2022

MFDS, Republic of Korea - Deadline for comments by 31 July 2022

MHLW/PMDA, Japan - Deadline for comments by 25 August 2022

MHRA, UK - Deadline for comments by 31 July 2022

NMPA, China - Deadline for comments by 15 July 2022

Swissmedic, Switzerland - Deadline for comments by 31 July 2022

TFDA, Chinese Taipei - Deadline for comments by 31 July 2022

ICH Q14 - Analytical Procedure Development (Step 2b)
ICH Q2(R2) - Validation of Analytical Procedures (Step 2b)

The Subject Matter Experts

We hope you enjoyed the webinar!

Learn more at redica.com