Joint Programming Initiative on Antimicrobial Resistance

Roadmap of Actions
2019-2024
## Contents

**Background and Introduction**
- The Joint Programming Initiative on Antimicrobial Resistance ........................................ 1
- The JPIAMR Strategic Research and Innovation Agenda (SRIA) ........................................... 1
- The JPIAMR Roadmap of Actions 2019-2024 ..................................................................... 2
- Activities and instruments .................................................................................................. 3
- JPIAMR joint actions for the years 2019-2024 ................................................................ 4

**Annex I. JPIAMR SRIA priority topics and research and innovation objectives** ........7

**Annex II. Description of JPIAMR Roadmap activities** ...................................................... 9

- Research Calls ................................................................................................................. 9
- Network Calls .................................................................................................................. 9
- Strategic workshops ....................................................................................................... 10
- JPIAMR-VRI ................................................................................................................... 11
Background and Introduction

Antibiotics have saved millions of lives throughout the many decades they have been in use. However, antimicrobial resistance (AMR) has become a global health challenge and the World Health Organisation (WHO) now considers AMR to be one of the greatest threats to public health, jeopardising the achievement of the Sustainable Development Goals. Increasing resistance to antibiotics affects human and animal health, food security and the environment. The urgency to act now, with a One Health approach, is highlighted by the estimation that without solutions the annual human deaths due to AMR are projected to be 10 million worldwide by 2050, surpassing casualties resulting from diabetes and cancer combined. To address this critical issue society needs to respond with concerted actions across all sectors.

The Joint Programming Initiative on Antimicrobial Resistance

The Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) is a global platform of 27 member nations¹ that coordinates national research funding and coordinates multi-sectorial AMR research and funding on a global scale. JPIAMR supports collaborative action for filling knowledge gaps on antimicrobial resistance with a One Health perspective.

JPIAMR supports new evidence and innovations that reduce the burden of antimicrobial resistance through coordinated global collaborative research in Europe and around the world with different activities and funding mechanisms. As well as accelerating the discovery of new antibacterial products, JPIAMR also supports research to better understand how resistance develops and spreads in the environment as well as the development of diagnostic tools, improved surveillance and intervention methods, and implementation of smarter strategies for using antibiotics in healthcare and agriculture.

JPIAMR recognises the need for a global approach to address AMR and has actively engaged countries beyond Europe as members and cooperates with key international organisations involved in AMR policy issues as well as international research funders.

The JPIAMR Strategic Research and Innovation Agenda (SRIA)

The JPIAMR Strategic Research Agenda (SRA) was published in 2014. In the years 2014-2018, the SRA guided national and international research priorities to curb AMR, and has provided a research framework for JPIAMR joint actions, as well as outlined key areas of AMR that should be addressed, and provided guidance for countries to align their AMR research agendas nationally and internationally. The SRA adopted the One Health approach and is included in the Global Action Plan on Antimicrobial Resistance (WHO, 2015) as a recommendation for national AMR action plans.

In 2019, JPIAMR published the JPIAMR Strategic Research and Innovation Agenda (SRIA²), which is an update of the SRA. The updated JPIAMR SRIA further emphasises the

---

¹ Members as of June 2019: Argentina, Belgium, Canada, Czech Republic, Denmark, Egypt, Estonia, Finland, France, Germany, Greece, Ireland, Israel, Italy, India, Japan, Netherlands, Norway, Poland, Romania, South Africa, South Korea, Spain, Sweden, Switzerland, Turkey and United Kingdom.
² www.jpiamr.eu/activities/sria/
One Health approach to address AMR and outlines six key priority topics within the AMR field: Therapeutics, Diagnostics, Surveillance, Transmission, Environment and Interventions (Figure 1).

**Figure 1.** The six priority topics of the JPIAMR SRIA: Therapeutics, Diagnostics, Surveillance, Transmission, Environment and Interventions.

Within each priority topic, a set of research objectives has been defined (Annex I). A shared common research and innovation agenda enhances multidisciplinary collaboration and ensures that knowledge gaps are quickly identified and incorporated in the joint funding activities.

**The JPIAMR Roadmap of Actions 2019-2024**

The JPIAMR Roadmap of Actions 2019-2024 will guide future joint transnational actions of the JPIAMR as well as to serve as an information resource for other strategic initiatives to support coordination and synergistic actions. The SRIA provides a framework for the joint actions outlined in this roadmap. However, since scientific developments and societal priorities are progressive, the JPIAMR Roadmap of Actions is considered to be a working document and is subject to change at the discretion of the JPIAMR Management Board.

An initial prioritisation of the SRIA research and innovation objectives that form the basis for the collaborative transnational initiatives was formulated at a prioritisation workshop involving scientists with expertise covering all priority areas of the SRIA. The workshop was held in Leiden, the Netherlands on the 6-7th December 2018. The actions defined at the workshop have been further refined and aligned with JPIAMR priorities by the JPIAMR Management Board and the JPIAMR Scientific Advisory Board.
Activities and instruments

The joint actions will be implemented through co-operative activities that re-align or link national investments to achieve increased impact and provide new funding. JPIAMR has, to date, held joint transnational calls for research projects and networks\(^3\), and convened workshops\(^4\). An overview of the past JPIAMR activities can be seen in Table 1.

In this Roadmap of Actions, JPIAMR will use different instruments to support and fund the identified research priorities. Among these are:

Research calls

Since 2014, JPIAMR has held annual joint transnational research calls (Table 1). The goal of the JPIAMR research calls is to foster and support multi-national translational research collaborations that can accomplish more than individual countries working independently.

Network calls

Network calls are a mechanism used by JPIAMR to enhance resource alignment and maximise existing and future efforts to combat AMR (Table 1). Within network calls, the funded networks may produce white papers, prospective views, guidelines, and/or best practice frameworks in order to identify key questions to be addressed or identify potential solutions to overcome barriers to AMR research studies. Supported networks should lead to outputs that will be of value to the broader AMR research community.

Networks are funded to enhance transnational communication and resource alignment and maximise existing and future efforts to combat AMR. The networks may produce white papers, prospective views, guidelines, and/or best practice frameworks and provide a consensus view of key questions to be addressed or potential solutions to overcome barriers to AMR research studies. Supported networks are guided by a network project plan with a 6-12 month timeframe within which to provide outputs that will be of value to the broader AMR research community.

Network Plus is a new funding instrument being developed by JPIAMR. This funding is for implementation of activities developed by Networks over a 1-2 year period.

Strategic Workshops

JPIAMR identifies and supports future joint actions through the organisation of strategic workshops. By bringing together experts from relevant fields relating to a specific topic, the JPIAMR workshops map the research landscape and identify knowledge gaps. All workshops produce reports and recommendations to JPIAMR.

The JPIAMR-VRI

To counter the unmet challenges of global coordination of research efforts to combat AMR, JPIAMR is developing the Virtual Research Institute (JPIAMR-VRI). The JPIAMR-VRI

\(^3\) [www.jpiamr.eu/supportedprojects/](www.jpiamr.eu/supportedprojects/)
\(^4\) [www.jpiamr.eu/activities/workshops/](www.jpiamr.eu/activities/workshops/)
will connect research networks and research performing organisations to implement AMR One Health research on the Strategic Research Agenda priority topics by increasing knowledge, diversity, collaborations and capability.

**JPIAMR joint actions for the years 2019-2024**

An overview of the planned JPIAMR joint actions for the years 2019-2024 are outlined in Table 2 and described in more detail in Annex II. The roadmap is to be regarded as a planning instrument for member states, funding agencies, researchers and other stakeholders and may be updated with additional activities. For updated information consult the JPIAMR website ([www.jpiamr.eu](http://www.jpiamr.eu)).
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research Calls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>InnovaResistance</td>
<td>InnovaResistance</td>
<td>Repurposing Neglected Antibiotics</td>
<td>Transmission and Selection of Resistance in Humans, Animals, and the Environment (ERAnet Cofund)</td>
<td>Prevention, control and intervention strategies for AMR infections</td>
<td>New targets, compounds and tools</td>
<td>Diagnostic and surveillance tools, technologies and methods to detect AMR</td>
</tr>
<tr>
<td><strong>Network Calls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMR Networks</td>
<td>AMR Networks</td>
<td>New frontiers in AMR research</td>
<td>Early discovery of new antibiotics</td>
<td>Surveillance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: All</td>
<td>Priority area: All</td>
<td>Priority area: All</td>
<td>Priority area: Therapeutics</td>
<td>Priority area: All</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Workshops</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional Latin America workshop</td>
<td>Diagnostics</td>
<td>New frontiers in AMR research</td>
<td>Early discovery of new antibiotics</td>
<td>JPIAMR Funded Networks workshop</td>
<td>Start-up workshop for Networks: Surveillance and Building the Foundation of the JPIAMR-VRI</td>
<td></td>
</tr>
<tr>
<td>Priority area: Surveillance</td>
<td>Priority area: Diagnostics</td>
<td>Priority area: All</td>
<td>Priority area: Therapeutics</td>
<td>Priority area: All</td>
<td>Priority areas: Surveillance and All</td>
<td></td>
</tr>
<tr>
<td>Diagnostics dynamics</td>
<td>Transatlantic collaboration on clinical trials</td>
<td>Environmental dimensions of AMR</td>
<td>The interplay between AMR surveillance and science</td>
<td>JPIAMR Virtual Research Institute</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: Transmission</td>
<td>Priority area: Therapeutics</td>
<td>Priority area: Environment</td>
<td>Priority area: Surveillance</td>
<td>Priority area: All</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>The interplay between AMR surveillance and science</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: Surveillance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPIAMR Virtual Research Institute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPIAMR Activity</td>
<td>2019/20</td>
<td>2020/21</td>
<td>2021/22</td>
<td>2022/23</td>
<td>2023/24</td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td><strong>Research Calls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPIAMR Network Plus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aquatic Pollutants</td>
<td>One Health interventions to prevent or reduce the development and transmission of AMR</td>
<td>Optimising existing drugs or drug combinations for the prevention and treatment of infections</td>
<td>Development of innovative, digital technologies for collection of microbiological and antibiotic data</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Priority area: Environment</td>
<td>Priority area: Transmission and Interventions</td>
<td>Priority area: Therapeutics</td>
<td>Priority area: Diagnostics and Surveillance</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Network Calls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JPIAMR Network Plus</td>
<td>Identifying knowledge gaps and best practices within One Health systems</td>
<td>To be determined</td>
<td>To be determined</td>
<td>Building Bridges between One Health areas to implement interventions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Priority area: All</td>
<td>Priority area: Transmission, Interventions and Environment</td>
<td></td>
<td>Priority area: Interventions</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Workshops</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One Health interventions to prevent or reduce the development and transmission of AMR</td>
<td>Development of a globally integrated One Health surveillance system of antibiotic resistant bacteria and antibiotic usage</td>
<td>Towards the global harmonisation of the analytical and clinical validation of in vitro diagnostic tests</td>
<td>Intervention standards and common practice</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: Transmission and Interventions</td>
<td>Priority area: Surveillance</td>
<td>Priority area: Diagnostics</td>
<td>Priority area: Interventions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harmonisation of non-antibiotic approaches and strategies to replace, control or minimise the use of antibiotics in early life animal husbandry</td>
<td>Final workshop for Networks: Surveillance and Building the Foundation of the JPIAMR-VRI</td>
<td>To be determined</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: Interventions</td>
<td>Priority area: Surveillance and All</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional Asia workshop</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: Therapeutics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>JPIAMR-VRI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hackathon</td>
<td>To be determined</td>
<td>Understanding One Health surveillance for students</td>
<td>Linking drug developers with end users</td>
<td>Linking early stage drug discovery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priority area: All</td>
<td></td>
<td>Priority area: Surveillance</td>
<td>Priority area: Therapeutics</td>
<td>Priority area: Therapeutics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Annex I. JPIAMR SRIA priority topics and research and innovation objectives

<table>
<thead>
<tr>
<th>Priority topic</th>
<th>Focus</th>
<th>Research and innovation objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Therapeutics</strong></td>
<td>Discovery of new antibiotics and therapeutic alternatives, and the improvement of current antibiotics and treatment regimens</td>
<td>• Find new antibiotics and targets &lt;br&gt; • Develop new chemical entities and scaffolds &lt;br&gt; • Improve pharmacokinetics and pharmacodynamics of antibiotics, including neglected antibiotics &lt;br&gt; • Use personalised medicine and artificial intelligence to improve therapies &lt;br&gt; • Develop alternatives for antibiotics &lt;br&gt; • Develop treatment protocols based on combination therapy using existing and new antibiotics &lt;br&gt; • Develop policy measures and economic stimuli to minimise barriers for the development, availability and introduction of new therapies and alternatives &lt;br&gt; • Assess how regulation modifies and influences production and use of antibiotics</td>
</tr>
<tr>
<td><strong>Diagnostics</strong></td>
<td>Development and improvement of diagnostics to improve the use of antibiotics and alternatives to antibiotics</td>
<td>• Improve the efficacy of new and existing diagnostic tools to more effectively distinguish between bacterial and non-bacterial infections, and/or detect antibiotic susceptibility &lt;br&gt; • Create support for the implementation of innovative technologies and linkage to data platforms promoting the use of narrow-spectrum antibiotics &lt;br&gt; • Improve the use of rapid diagnostics in appropriate One Health settings &lt;br&gt; • Improve understanding and explore ways to overcome behavioural and socio-economic barriers limiting the adoption and use of rapid diagnostics</td>
</tr>
<tr>
<td><strong>Surveillance</strong></td>
<td>Optimisation of surveillance systems to understand the drivers and burden of antimicrobial resistance in a One Health perspective</td>
<td>• Improve and standardise AMR surveillance systems, from sampling to data analysis including sampling frame, tools, methodology and reporting &lt;br&gt; • Strengthen the use of surveillance data to identify human and non-human reservoirs of AMR &lt;br&gt; • Optimise the use of surveillance data to estimate burden and to assess the impact of interventions &lt;br&gt; • Develop novel techniques to supplement and promote the exchange of surveillance data &lt;br&gt; • Improve and standardise the surveillance of antibiotic use</td>
</tr>
<tr>
<td>Priority topic</td>
<td>Focus</td>
<td>Research and innovation objectives</td>
</tr>
<tr>
<td>---------------</td>
<td>-------</td>
<td>----------------------------------</td>
</tr>
</tbody>
</table>
| **Transmission** | Understanding and preventing the transmission of antimicrobial resistance | • Unravel the complex dynamics of selection and transmission of antimicrobial resistance  
• Identify factors responsible for the persistence and spread of resistant organisms and resistance elements  
• Determine the impact on AMR of different systems of healthcare, animal production, global trade and environmental pollution and contamination |
| **Environment** | The role of the environment in the selection and spread of antimicrobial resistance | • Determine and model the contribution of contamination sources, environmental reservoirs and exposure routes on the emergence and spread of AMR  
• Evaluate the relationship between AMR and the environment, climate change, and pollution  
• Assess the potential impact of industrial systems on AMR in the environment  
• Develop innovative technological, policy, social, economic and regulatory approaches to mitigate AMR in the environment |
| **Interventions** | Investigation and improvement of infection prevention and control measures in One Health settings | • Develop innovative interventions aimed to prevent and control the spread of AMR in a One Health perspective  
• Investigate the effectiveness of AMR prevention and control strategies to increase uptake and acceptance in One Health settings  
• Assess the effectiveness and cost-effectiveness of specific AMR prevention and control practices, considering different geographic and socio-economic settings  
• Optimise implementation strategies, including drivers for and barriers to behavioural change, to reduce AMR  
• Understand the prescription behaviours contributing to the responsible and prudent use of antimicrobials  
• Assess educational and training programmes to enhance antibiotic stewardship |
Annex II. Description of JPIAMR Roadmap activities

Research Calls

• *Aquatic Pollutants*
  Priority area: Environment

  JPIAMR is collaborating with JPI Water and JPI Oceans to draft a research call to fill existing key knowledge gaps regarding the environmental behaviour of new and emerging pollutants as well as pathogens in inland waters and the marine environment, and their impacts on ecosystems and human health. Further details of this call will be available in late 2019.

• *One Health interventions to prevent or reduce the development and transmission of antimicrobial resistance (AMR)*
  Priority area: Transmission and Interventions

  In 2019, JPIAMR will begin preparations for the 2020/2021 call for One Health interventions to prevent or reduce the development and transmission of antimicrobial resistance (AMR). More information will be available on this call in the second half of 2020.

• *Optimising existing drugs or drug combinations for the treatment of infections and/or prevention of the emergence/spread of resistance caused by priority pathogens on the WHO and OIE lists, including and up to preclinical development*
  Priority area: Therapeutics

  This research call will aim to support projects to understand the optimal combination(s) of antibacterial agents to treat infections mainly caused by multidrug resistant bacteria.

• *Development of innovative, digital technologies for collection of microbiological and antibiotic data to support and inform clinical decision making (algorithms) and One Health surveillance, to promote prudent and rational use of antibiotics*
  Priority area: Diagnostics and Surveillance

  The call will focus on the development of evidence-based guidance building on rapid diagnostics, to promote prudent and rational use of antibiotics.

Network Calls

• *JPIAMR Network Plus*
  Priority area: All

  The JPIAMR Network Plus Call is a follow up mechanism to JPIAMR Network calls to support implementation of planned activities. Further development of the Network Plus instrument will be conducted in 2019.
• **Identifying knowledge gaps and developing best practices and innovative technological, policy, social, economic and regulatory approaches to monitor the transmission of antimicrobial resistance to, from and within One Health systems**

Priority area: Transmission, Interventions and Environment

This network call will support networks to develop, improve, standardise, and/or compare existing and novel research methodologies, tools, and models focusing on identification of One Health AMR transmission routes and drivers, and quantification of AMR burden.

• **Building bridges between One Health areas to develop guidance and shared measures and standards to assess and implement interventions**

Priority area: Interventions

This Network call will focus on linking different One Health areas to facilitate transfer of ideas and knowledge and foster system-wide thinking when it comes to AMR interventions.

**Strategic workshops**

• **One Health interventions to prevent or reduce the development and transmission of antimicrobial resistance (AMR)**

Priority area: Transmission and Interventions

In 2020 a scoping workshop will be held for the development of the 2020/2021 call for One Health interventions to prevent or reduce the development and transmission of antimicrobial resistance (AMR).

• **Harmonisation of non-antibiotic approaches and strategies to replace, control or minimise the use of antibiotics in early life animal husbandry**

Priority area: Interventions

The workshop will aim to provide intervention recommendations/overview of promising strategies considering socio-economic and clinical outcomes and practical implementation. Information from this workshop could also feed into scoping the 2020/21 call for the One Health interventions to prevent or reduce the development and transmission of AMR as listed above.

• **Regional Asia workshop**

Priority area: Therapeutics

A regional workshop for scientists in Asia will be held in South Korea in 2019, with a focus on therapeutics and alternatives to antibiotics.

• **Development of a globally integrated One Health surveillance system of antibiotic resistant bacteria and antibiotic usage with the goal of inter-sectoral coordination including the healthcare setting and community**
Priority area: Surveillance

In alignment with the final workshop for ongoing funded Networks within the 2018 JPIAMR Surveillance call, this workshop will focus on the development of a globally integrated human, animal and environmental surveillance system of antibiotic resistant bacteria and antibiotic usage with the goal of inter-sectoral coordination including the healthcare setting and community.

- **Final workshop for Networks: Surveillance and Building the Foundation of the JPIAMR-VRI**

Priority area: Surveillance and All

Networks funded within the JPIAMR Network Calls for Surveillance and Building the Foundation of the JPIAMR-VRI will meet to discuss outcomes from Network activities and alignment of future activities.

- **Towards the global harmonisation of the analytical and clinical validation of in vitro diagnostic tests used in the context of antimicrobial resistance, bringing together relevant stakeholders including academia, industry, health care providers, payers, regulators, and international organisations**

Priority area: Diagnostics

A new EU directive will become operational regarding the requirements of performance and regulatory processes. This workshop will map existing regulatory and pricing processes, and the feasibility of sharing technology.

- **Intervention standards and common practice**

Priority area: Interventions

This workshop will focus on sharing common practices, policies and standards regarding innovative AMR interventions considering a system-wide perspective, considering the prudent use of antibiotics and reduction of AMR spread in the One Health context.

**JPIAMR-VRI**

- **Hackathon: Brainstorming session to find new ways to tackle AMR**

Priority area: All

The AMR hackathon will engage young researchers to generate innovative ideas and solutions that could lead to new ways to tackle AMR that potentially could be a future JPIAMR action within the JPIAMR-VRI.

- **Understanding One Health surveillance for clinical practice for medical, veterinary and pharmacy students**

Priority area: Surveillance
This action will support capacity building of medical, veterinary and pharmacy students in the area of AMR surveillance.

• **Linking drug developers with end users**  
  Priority area: Therapeutics

  This action will engage diverse stakeholders including discovery researchers, and preclinical drug developers both from academia and the industry (including start-ups and SMEs), clinicians, as well as economists, public health experts and knowledgeable healthcare/veterinary investors.

• **Linking early stage drug discovery**  
  Priority area: Therapeutics

  This action supports capacity building in the area of early drug discovery for the discovery of new targets, compound, and alternatives. It is anticipated that this action could include a mobility network as a tool to integrate and facilitate the exchange between existing PhD programmes for building technical skills and sharing knowledge and resources for drug discovery.