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Horizon Scanning of Biotechnologies with Chemical and Biological Defense Applications: A 12-Month Pilot Study

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February 2023
Approved for public release;
distribution unlimited.
IDA Document NS D-33388
Log: H 23-000037

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About This Publication
This work was conducted by the Institute for Defense Analyses under contract HQ0034-19-D-0001, project DC-6-5047, "Biotechnology Horizon Scanning" for the Advanced and Emerging Threats Division in the Research and Development (R&D) Directorate of the Chemical and Biological Technologies, Joint Science and Technology Office, Defense Threat Reduction Agency (DTRA-JSTO). The views, opinions, and findings should not be construed as representing the official position of either the Department of Defense or the sponsoring organization.

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Executive Summary

Horizon scanning is an effort to identify and analyze signals of change based on past observations and current trends. In order to fulfill its mission to prevent technical surprise from advanced chemical and biological threats, the Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department, Advanced and Emerging Threat Division sponsored the Institute for Defense Analyses (IDA) to develop and execute a methodology for biotechnology horizon scanning. Over a 12-month period, the IDA team scanned open source literature for surprising developments in biotechnology that had the potential to benefit or threaten the warfighter within five-to-ten years. At the end of each month, the technologies and research identified by the IDA team were summarized in a report that assessed their impact to technical surprise, technical maturity, and potential battlefield applications. Quarterly, the ten technologies and findings of the highest impact to technical surprise and/or greatest relevance to the Chemical and Biological Defense Program (CBDP) were further analyzed to characterize the potential risks and rewards to U.S. chemical and biological defense capabilities in the next five-to-ten years. Finally, results from the 12-month pilot study were collated into a final paper that analyzes the trends observed over the course of the study, highlighting a few key areas of interest to the sponsor.

With feedback from DTRA, the IDA team divided research into nine categories: brain-computer interfaces, biomarkers/wearables, diagnostics, dual use, environmental sensors, injury recovery, non-medical mission support, disease and injury prevention, and vaccines/therapeutics. During the course of this pilot study, IDA identified 157 findings or technologies with potential impact to technical surprise that could be used in applications to benefit or threaten the warfighter within five-to-ten years. The application categories with the most findings overall were vaccines/therapeutics, injury recovery, and enabling dual use. The category with the most high-impact studies during the pilot study period was enabling dual use.

Future efforts will be conducted to increase the breadth of material covered by our technological horizon scanning. For example, automation is being considered to complement subject matter expertise in expanding the scope of the effort, both in terms of the number of articles and in the application types that could be examined, to include non-bio-based technologies that are relevant to CBDP capabilities. In addition, continuing the horizon scanning effort over time will likely improve forecasting ability and allow for retrospective analysis of trends.

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INTRODUCTION

Horizon scanning is an effort to identify and analyze signals of change based on past observations and current trends. In order to fulfill its mission of preventing technical surprise from advanced chemical and biological threats, the U.S. Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department, Advanced and Emerging Threat Division sponsored the Institute for Defense Analyses (IDA) to develop and execute a methodology for biotechnology horizon scanning and write monthly and quarterly reports describing new biotechnology research.

MONTHLY REPORT METHODOLOGY

The IDA team continuously scanned open source literature for innovative biotechnologies with the potential to effect warfighter performance within 5-10 years (**Fig. 1**). At the end of each month, the technologies and research identified by the IDA team were summarized in a report that assessed their potential battlefield applications (**Fig. 2**), impact to technical surprise (**Fig. 3**), and technical maturity. We defined technical surprise as an unexpected development in biotechnology, with the different levels of potential impact presented in **Fig. 3**.

Figure 1: Horizon Scanning Methodology Flowchart

1. Source gathering
   - Monitor scientific literature
     - High impact journals (e.g. Nature, Cell, Science, PNAS)
     - News articles and press releases
     - Aggregator websites
2. Technology assessment
   - Identify applications (**Fig. 2**), potential impact to technical surprise (**Fig. 3**), and technical maturity
3. Team corroboration:
   - Compare/reconcile independent assessments between IDA team members
4. Compilation of monthly report
   - Monthly report disseminated through sponsor's office to stakeholders

Figure 2: Battlefield Application Categories and Examples

Application Area	Example Technology
Brain-Computer Interface (BCI)	Decoding speech from non-invasive brain recording
Biomarkers/Wearables	A tissue-like neurotransmitter sensor for the brain and gut
Diagnostics	Enteric viruses replicate in salivary glands
Enabling Dual Use	A sustainable mouse karyotype created by programmed chromosome fusion
Environmental Sensors	Directed evolution and selection of biostable L-DNA aptamers with mirror-image DNA polymerase
Injury Recovery	Patch grafting of organoids into solid organs to correct disease states
Non-Medical Mission Support	Super-resolution wearable electrotactile rendering system
Prevention (disease, injury)	Continuous air purification by aqueous interface filtration and absorption
Vaccines/Therapeutics	A bacterial pan-genome makes gene essentiality strain-dependent and evolvable

MONTHLY REPORT METHODOLOGY (ctd.)

Figure 3: Assessed Levels of Impact to Technical Surprise*

Potential Impact to Technical Surprise	Technology Type	Technology Description
No impact	Novel	Technology that builds upon an existing biotechnology product or discovery in an anticipated way and/or rate
Low impact	Catalyst	Technology that alters rate of change of technical development or rate of improvement of 1 or more technologies
Low-Medium	Enhancer	Technology that modifies existing biotechnologies; tipping interest in tech across critical threshold
Medium impact	Breakthrough	Discovery or technology that changes the fundamental understanding of nature or makes possible something that previously seemed impossible (or improbable)
High impact	Disruptive	Innovative tech that triggers sudden and unexpected effects

*Impact levels developed from the National Research Council's *Persistent Forecasting of Disruptive Technologies* report. [1]

QUARTERLY REPORT METHODOLOGY

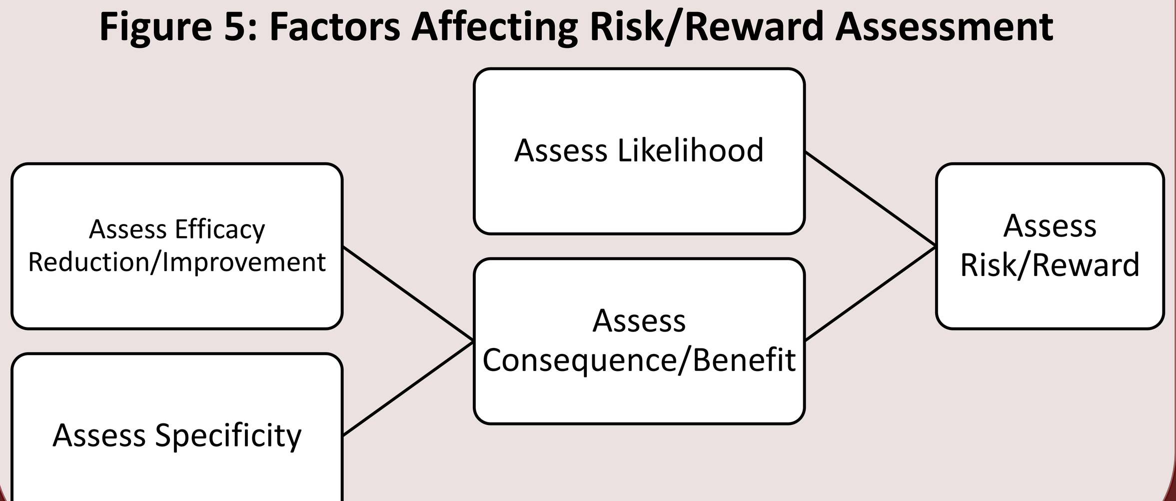
The 10 technologies and findings of the highest impact to technical surprise and/or greatest relevance to the Chemical and Biological Defense Program (CBDP) from the monthly reports were further analyzed to characterize the potential risks and rewards to U.S. CBDP capabilities in the next 5-10 years (**Fig. 4**).

Figure 4: Quarterly Report Methodology Flowchart

1. Select research for quarterly focus areas
   - Top 10 technologies of the quarter that are most disruptive to their respective domain or most relevant to CBDP capabilities
2. Indicate example application(s) achievable within 5-10 years
   - Build off monthly reports using subject matter expert (SME) judgement of defense-relevant applications
3. Describe risks/rewards to CBDP capabilities associated with such application(s) (Fig. 5-9)
   - CBDP missions are to understand, protect, and mitigate the effects of chemical and biological agents
4. Characterize battlefield advantages & implications for CBDP
   - Describe broad strategic and CBDP implications, including implications that may not be relevant to CBDP but could alter warfighter performance.
5. List technical limitations
   - Describe limitations of required technologies for application, technology itself, and in the demonstration of the technology (e.g. limited clinical trials, animal studies only)

We considered risk/reward to be a product of likelihood and consequence/benefit (**Fig. 5**). Our risk assessment methodology was informed by the Joint Risk Assessment Methodology. [2]

Figure 5: Factors Affecting Risk/Reward Assessment



QUARTERLY REPORT METHODOLOGY (ctd.)

We defined Likelihood as the probability that the identified application of the technology sufficiently matures within the next 5-10 years, assuming that other technologies required for this use do not develop past their current states **(Fig. 6)**.

Figure 6: Assessed Likelihood Levels

Low	≤25% Probability • Technology cannot be expected to mature due to limitations or lack of evidence • Application is dependent on other technologies, none or few of which in their current state would fulfill this requirement
Medium	25%-75% Probability • No strong indication to whether a technology will mature • Application is dependent on other technologies, several of which in their present state would fulfill this requirement
High	≥75% Probability • Technology can be expected to sufficiently mature • Application is dependent on other technologies, all or most of which would fulfill this requirement in their present state.

We defined Consequence/Benefit as the magnitude of change (damage or improvement) to CBD capabilities. Magnitude of change is a function of Efficacy (how much the capabilities could be affected) and specificity (how many capabilities could be affected). Efficacy and Specificity levels are defined in **Fig. 7**.

Figure 7: Efficacy and Specificity Levels

Efficacy	
Limited	Limited to no change in the performance of the capability
Moderate	Moderate change in the performance of the capability
Significant	Creation of capability that previously did not exist

Specificity	
Narrow	Affects 1 CB agent
Multi-target	Affects multiple CB agents (e.g., VEE + EEV + WEEV)
Broad	Affects a "class" of CB agents (e.g., all Fourth Generation Agents, FGAs)

We then combined the Efficacy and Specificity levels into a single Consequence/Benefit level using the matrix presented in **Fig. 8**. For illustrative purposes, we are showing the Consequence matrix, but an analogous matrix exists for Benefit.

Figure 8: Consequence Matrix

	Efficacy Reduction		
Specificity of Capability	Limited	Moderate	Significant
Narrow-spectrum	Low	Low	Medium
Multi-target	Low	Medium	High
Broad-spectrum	Medium	High	High

Likelihood and Consequence/Benefit are combined into Risk/Reward using the matrix presented in **Fig. 9**. For illustrative purposes, we are showing the Risk matrix, but an analogous matrix exists for Reward.

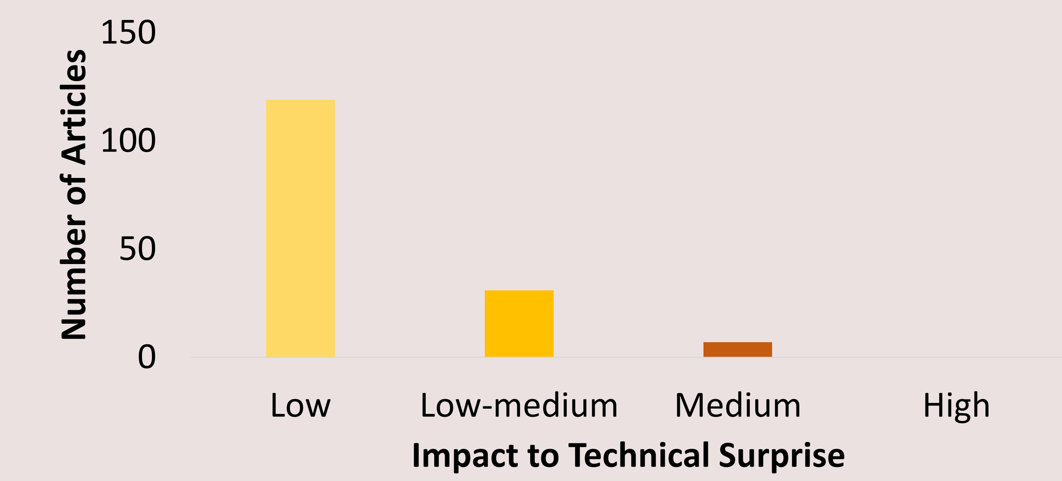
Figure 9: Risk Matrix

Consequence				
	High	Medium	High	V. High
	Medium	Low	Medium	High
	Low	V. Low	Low	Medium
		Low	Medium	High
		Likelihood		

OVERALL RESULTS

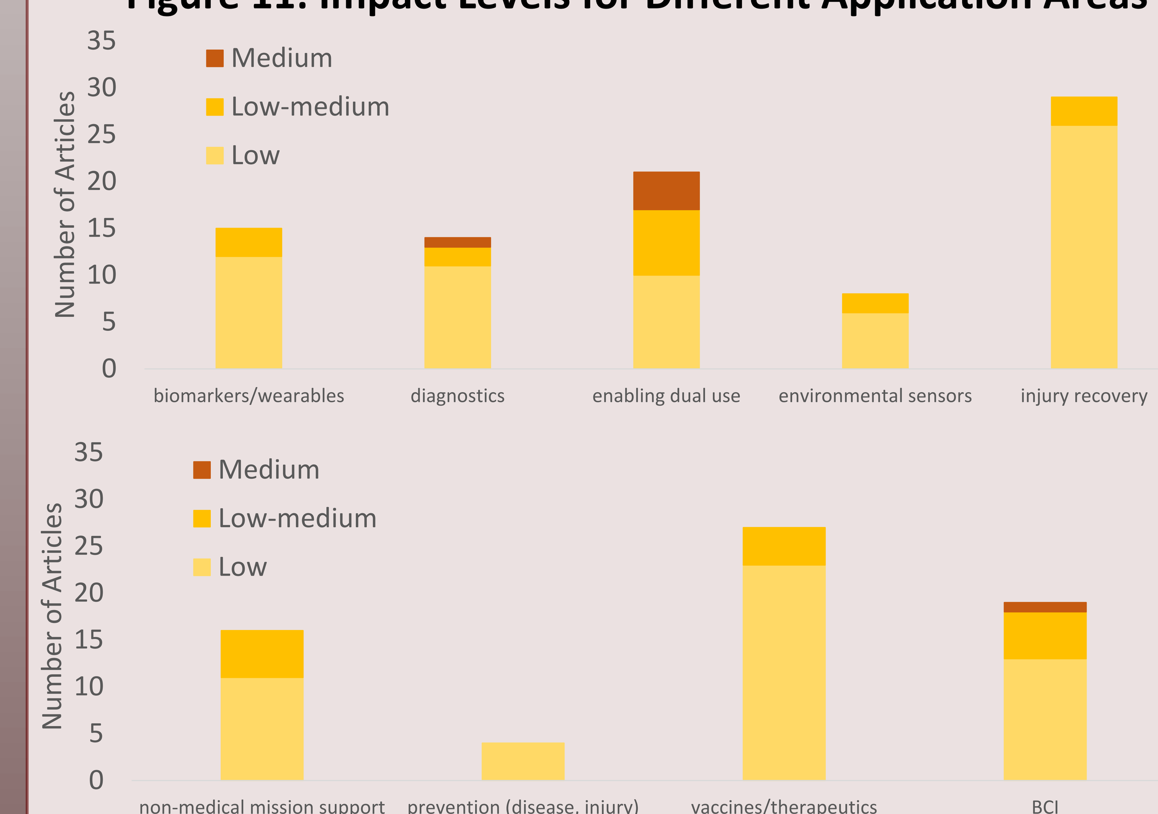
Finally, results from the 12-month pilot study were collated into a final paper that analyzes the trends observed over the course of the study, highlighting a few key areas of interest to the U.S. CBDP. During the course of the study, 157 articles were identified and their Impact levels are presented in **Fig. 10**. No articles with an Impact above Medium were encountered during the pilot study.

Figure 10: Assessed Impact to Across All Articles



The application categories with the most findings overall were vaccines/therapeutics, injury recovery, and enabling dual use (**Fig. 11**). Additionally, the category with the most high impact studies during the pilot study period was enabling dual use.

Figure 11: Impact Levels for Different Application Areas



FUTURE DIRECTIONS

Future efforts will be conducted to improve the breadth of material covered by our technological horizon scanning. For example, automation is being considered to complement subject matter expertise in expanding the scope of the effort, both in terms of the number of articles and application types that could be examined, to include non-bio-based technologies that are relevant to CBDP capabilities. Additionally, continuing the horizon scanning effort over time will likely improve forecasting ability and allow for retrospective analysis of trends.

REFERENCES

[1] National Research Council, *Persistent Forecasting of Disruptive Technologies* (Washington, DC: National Academies Press, 2010).

[2] Chairman of the Joint Chiefs of Staff, CJCSM 3105.01A, "Enclosure B: Joint Risk Analysis Methodology (JRAM)," *Joint Risk Analysis Methodology* (Washington, DC: October 2021).

REPORT DOCUMENTATION PAGE	Form Approved OMB No. 0704-0188

1. REPORT DATE (DD-MM-YY)	2. REPORT TYPE	3. DATES COVERED (From – To)
xx-02-2023	Final	

4. TITLE AND SUBTITLE *Horizon Scanning of Biotechnologies with Chemical and Biological Defense Applications: A 12-Month Pilot Study*	5a. CONTRACT NO. HQ0034-19-D-0001 5b. GRANT NO. 5c. PROGRAM ELEMENT NO(S).
6. AUTHOR(S) Ashley L. Farris Janet Marroquin Pineda Kristen Bishop Robert Cubeta Jay Shah Jason Zhang	5d. PROJECT NO. 5e. TASK NO. DC-6-5047 5f. WORK UNIT NO.
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Institute for Defense Analyses 730 E.Glebe Rd Alexandria, VA 22305	8. PERFORMING ORGANIZATION REPORT NO. IDA Document NS D-33388 Log: H 23-000037
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) DTRA :8725 John J Kingman Road Fort Belvoir, VA 22060	10. SPONSOR'S / MONITOR'S ACRONYM(S) DTRA 11. SPONSOR'S / MONITOR'S REPORT NO(S).

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The Advanced and Emerging Threat Division in the U.S. Defense Threat Reduction Agency's Chemical and Biological Technologies Department sponsored the Institute for Defense Analyses (IDA) to develop and implement a biotechnology horizon scanning method in support of their mission to mitigate the risk of technical surprise. For this pilot study, the IDA team continuously monitored the open source scientific literature to identify innovative biotechnologies and research with the potential to affect warfighter performance in the next five-to-ten years. Each month, the team assessed the impact to technical surprise for all identified biotechnologies and research studies relevant to warfighter performance, provided a qualitative measure of technical maturity, and identified applications relevant to chemical and biological defense capabilities. Each quarter, the team conducted a risk/reward assessment for the applications identified for the ten research findings with the highest impact to technical surprise. Finally, the team collated the results from the 12-month pilot study into a final report that analyzes the trends observed within the key areas of interest to the sponsor.

15. SUBJECT TERMS

Emerging technologies; biotechnology; horizon scanning; chemical and biological defense

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NO. OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			: Giselle Roman Hernandez
U	U	U	U	10	19b. TELEPHONE NUMBER (Include Area Code) 571-616-5701

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