Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
MicroGuide-2

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product

( ) Clinical investigation or other study of a medical device

( ) Combined trial of an investigational medicinal product and an investigational medical device

( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

( ) Basic science study involving procedures with human participants

( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

( ) Study involving qualitative methods only

( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

( ) Study limited to working with data (specific project only)

( ) Research tissue bank

( ) Research database

If your work does not fit any of these categories, select the option below:

(●) Other study

2a. Will the study involve the use of any medical device without a UKCA/CE UKNI/CE Mark, or a UKCA/CE UKNI/CE marked device which has been modified or will be used outside its intended purposes?

(●) Yes ( ) No

2b. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ( ) Yes (●) No

b) Will you be taking new human tissue samples (or other human biological samples)? ( ) Yes (●) No

c) Will you be using existing human tissue samples (or other human biological samples)? ( ) Yes (●) No

3. In which countries of the UK will the research sites be located? *(Tick all that apply)*

- [x] England
- [ ] Scotland
- [ ] Wales
- [ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- (•) England
- ( ) Scotland
- ( ) Wales
- ( ) Northern Ireland
- ( ) This study does not involve the NHS

4. Which applications do you require?

- [x] IRAS Form
- [ ] Confidentiality Advisory Group (CAG)
- [ ] Her Majesty's Prison and Probation Service (HMPPS)

Most research projects require review by a REC within the UK Health Departments' Research Ethics Service. Is your study exempt from REC review?

( ) Yes (•) No

5. Will any research sites in this study be NHS organisations?

(•) Yes ( ) No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out the research e.g. NHS support costs) for this study provided by a NIHR Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), NIHR Patient Safety Translational Research Centre (PSTRC), or an NIHR Medtech and In Vitro Diagnostic Co-operative (MIC) in all study sites?

Please see information button for further details.

( ) Yes (•) No

Please see information button for further details.

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) Support and inclusion in the NIHR Clinical Research Network Portfolio?

Please see information button for further details.

(•) Yes ( ) No

The NIHR Clinical Research Network (CRN) provides researchers with the practical support they need to make clinical studies happen in the NHS in England e.g. by providing access to the people and facilities needed to carry out research "on the ground".

If you select yes to this question, information from your IRAS submission will automatically be shared with the NIHR CRN. ***Submission of a Portfolio Application Form (PAF) is no longer required.***

6. Do you plan to include any participants who are children?

○ Yes ◉ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

○ Yes ◉ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Other research

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
MicroGuide-2

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

MicroGuide-2: A randomized controlled trial of the impact of MicroGuide™ computerized decision support modules on antimicrobial prescribing behaviours and clinical outcomes.

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Dr	Philip	Scott
Post	Reader in Health Informatics		
Qualifications	MSc PhD		
ORCID ID	0000 0002 6289 4260		
Employer	University of Portsmouth		
Work Address	Buckingham Building Lion Terrace Portsmouth		
Post Code	PO1 3HE		
Work E-mail	philip.scott@port.ac.uk		
* Personal E-mail			
Work Telephone	02392846378		
* Personal Telephone/Mobile	07810826522		
Fax			

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

Title	Forename/Initials	Surname
Dr	Philip	Scott

Address	Buckingham Building Lion Terrace Portsmouth
Post Code	PO1 3HE
E-mail	philip.scott@port.ac.uk
Telephone	07810826522
Fax	

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	PHT/2020/43
Sponsor's/protocol number:	8543
Protocol Version:	2.4
Protocol Date:	12/01/2021
Funder's reference number (enter the reference number or state not applicable):	N/A
Project website:	

Registry reference number(s):
The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

International Standard Randomised Controlled Trial Number (ISRCTN):

ClinicalTrials.gov Identifier (NCT number):

Additional reference number(s):

Ref.Number Description	Reference Number

A5-2. Is this application linked to a previous study or another current application?

(●) Yes ( ) No

Please give brief details and reference numbers.
MicroGuide study 1: 18/HRA/0256

The initial (MicroGuide-1) study explored user experience and changes in trends of antibiotic prescribing after implementation of the basic “browse version” of the MicroGuide App, which provides easy access to local antibiotic treatment guidelines. The MicroGuide-2 study will investigate the impact of an additional functionality within the App - algorithmic decision support for specific common infections.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments’ Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.*

The World Health Organisation says that "antibiotic resistance is one of the biggest threats to global health, food security, and development" (WHO, 2020). The major cause of resistance is over-use of antibiotics, either because they are available without medical prescription or from over-prescribing. To address this problem, the policy of "antimicrobial stewardship" has been developed. This means "promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness" (NICE, 2015). MicroGuide™ is an app to help hospital prescribers select the appropriate antimicrobial drug, by presenting hospital medicine guidelines in a user-friendly way. MicroGuide has the ability to create decision support modules (DSMs) for particular conditions, so that prescribers can answer a series of conditional questions about factors such as disease severity, allergies, resistance risks and pregnancy status to be guided to a recommended choice of drugs or in some cases to seek further microbiology specialist advice. This study is to evaluate whether implementing decision support modules within the MicroGuide application will improve the quality of antimicrobial prescribing and clinical outcomes. The study is sponsored and funded by Merck Sharp & Dohme (UK) Ltd. Up to 24 NHS Trusts and 30 NHS staff members will take part in this study.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, R&D office or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

The lead clinician responsible for implementation of the app at each eligible organisation will be invited by Horizon Strategic Partners (MicroGuide software developers) to participate and, if they give consent, their contact details will then be forwarded to the research team to formally recruit them to the study. It is anticipated that the majority will be specialist antibiotic pharmacists, consultant medical microbiologists or infectious diseases physicians. The lead clinicians will be required to obtain organization-level consent for study participation, specifically to be randomized to mandatory implementation of decision support modules for five common infections within the MicroGuide app or to continue using the standard version of the MicroGuide application (i.e. browse format) for the five common infections. It is anticipated that organization level consent will require approval by an internal governance committee such as the hospital Antimicrobial Stewardship Committee or Drug & Therapeutics Committee or equivalent. The lead clinicians will be asked to consent to analysis of app use statistics and aggregated Trust-level antibiotic prescribing (from the RxInfo Define software), resistance (from Public Health England Fingertips website) and clinical outcome data (from NHS Digital).

Individual clinicians in the intervention arm will be free to choose to utilise the MicroGuide application or not, but if they do opt to use it then they will only have the version with decision support modules. Clinicians at all study sites will continue to be able to access versions of treatment guidelines in a browse format (e.g. Microsoft Word document or PDF) on their hospital intranet. Decisions about selection of hospital IT applications are routinely made by Trust management, so this is no different to any other IT implementation in that respect.

For the avoidance of doubt, no administration of any therapeutic or prophylactic agent is required in this protocol. Individual patient consent will not be required because the study will collect and analyse aggregated outcome data at organization level.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- ☐ Case series/ case note review
- ☐ Case control
- ☐ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☑ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study

- [ ] Laboratory study
- [ ] Metanalysis
- [x] Qualitative research
- [ ] Questionnaire, interview or observation study
- [x] Randomised controlled trial
- [ ] Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

To determine whether there are statistically significant and clinically significant changes in broad-spectrum antimicrobial prescribing (specifically, drugs from the carbapenem family of antibiotics) caused by implementation of decision support modules for five common infections within the MicroGuide application.

Broad-spectrum antibiotics are active against a broad range of bacteria, including bacteria resistant to narrow-spectrum antibiotics. Broad-spectrum antibiotics should only be prescribed when patients are at risk of antibiotic-resistant infection.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

To determine whether there are statistically significant and clinically significant changes in patterns of piperacillin-tazobactam prescribing (another broad-spectrum antibiotic) caused by implementation of MicroGuide decision support modules (DSMs) for five common infections.

To determine whether there are statistically significant and clinically significant changes in antimicrobial resistance rates (E. coli resistance to piperacillin-tazobactam) caused by implementation of MicroGuide DSMs for five common infections.

To analyse the opinions of MicroGuide DSM users about the effectiveness and usability of the modules and how they affect their prescribing practice.

To determine how quickly the MicroGuide DSMs are adopted in the intervention arm, whether usage is sustained over the study period and whether there is variation in patterns of usage by site or condition.

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Clinical decision support (CDS) does not automatically improve practice. CDS is often ignored, over-ridden or has unintended consequences. However, well-designed and well-implemented CDS can be welcomed by clinicians and demonstrate improved guideline adherence. Four systematic reviews (including two meta-analyses) of the impact of CDS on antimicrobial prescribing have been published within the last four years. Most of the identified studies are non-randomized and of low methodological quality and considerable heterogeneity in CDS systems was reported. CDS was associated with an increase in appropriate selection of effective (active in vitro against isolated pathogenic microorganism) antimicrobial therapy, a reduction in mortality, decreased length of hospital stay, a reduction in treatment course length and reduced overall antimicrobial consumption.

Some physicians are dubious about the value of CDS for antimicrobial prescribing and so far there is limited evidence to show significant impact upon usage of broad-spectrum antimicrobial drugs or associated clinical outcomes. The purpose of this study is to definitively answer the question whether CDS delivered through the widely-adopted MicroGuide™ application can be shown to improve the clinical effectiveness and appropriateness of antimicrobial prescribing.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

The study is a two-arm parallel randomized controlled trial (RCT) with supporting qualitative study of clinician experience.

The setting is acute hospital NHS Trusts in England in the middle band of carbapenem prescribing volume (defined

below), measured as Defined Daily Doses (DDDs) per thousand admissions. Carbapenem prescribing volume has been selected as the primary outcome variable because it is widely accepted as a key indicator for antimicrobial stewardship and the aggregated data are readily available from PHE (quarterly, public data) and RxInfo (monthly, data available to subscribing NHS Trusts) to support power calculations and trial analysis. The prescribing volume is expressed as World Health Organisation DDDs per thousand admissions as a standardized reporting unit.

Due to the wide variation in the primary outcome variable between NHS Trusts, the study will recruit from the middle band of carbapenem prescribing so as to limit variance and increase the power of the study to detect significant change.
NHS Trust is the unit of analysis as the primary outcome data are only available at organizational unit level.

All NHS Trusts in the middle band that use MicroGuide will be invited to participate in the RCT. Participating sites will be randomized to intervention or control arms. Recruiting from the middle band of carbapenem prescribing potentially represents a threat to the generalisability of the study findings, but it is anticipated that any beneficial impact of the DSMs to acute NHS Trusts in the middle band will be amplified in those Trusts in the higher quintiles.

Primary exposure is deployment of the decision-support module (DSM) functionality within the MicroGuide app for five common infections for the 12-month period following Trust implementation of the MicroGuide DSMs. A full year is stipulated as a minimum requirement to guarantee robust analysis of a time series incorporating seasonal variations.

The primary outcome data collection will comprise monthly data releases from RxInfo (https://www.rx-info.co.uk/products/define/) and quarterly public data releases from Public Health England (PHE). Prescribing data are aggregated at hospital level and individual patient prescribing data are not available or required.

The tertiary quantitative outcome data collection will comprise a 12-month extract from NHS Digital based on the defined list of coded diagnoses. Clinical outcome data will be aggregated by NHS Trust for the cohort of patients with a coded diagnosis of one or more of five common infections (community-acquired pneumonia; hospital-acquired pneumonia; urinary tract infection; cellulitis; biliary tract infection). Note: The NHS Digital data set does not and cannot contain identifiers or outcome data for individual patients nor treatment assignment details for individual patients. Individual diagnoses or antimicrobial class(es) will not be identified in the data set.

Qualitative data will be collected from interviews with prescribers using MicroGuide.

Note: References to PHE should be understood to include whatever successor body assumes its duties for publishing antimicrobial prescribing and resistance data.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- ☐ Design of the research
- ☐ Management of the research
- ☐ Undertaking the research
- ☐ Analysis of results
- ☐ Dissemination of findings
- ☑ None of the above

Give details of involvement, or if none please justify the absence of involvement.
MicroGuide-1 had specific patient and public involvement activities. We have held a patient and public involvement workshop about trust and governance issues for clinical decision support generally, not specific to MicroGuide.

We are seeking funding to support a patient and public involvement workshop for MicroGuide-2.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A15. What is the sample group or cohort to be studied in this research?

Select all that apply:

- [ ] Blood
- [ ] Cancer
- [ ] Cardiovascular
- [ ] Congenital Disorders
- [ ] Dementias and Neurodegenerative Diseases
- [ ] Diabetes
- [ ] Ear
- [ ] Eye
- [x] Generic Health Relevance
- [ ] Infection
- [ ] Inflammatory and Immune System
- [ ] Injuries and Accidents
- [ ] Mental Health
- [ ] Metabolic and Endocrine
- [ ] Musculoskeletal
- [ ] Neurological
- [ ] Oral and Gastrointestinal
- [ ] Paediatrics
- [ ] Renal and Urogenital
- [ ] Reproductive Health and Childbirth
- [ ] Respiratory
- [ ] Skin
- [ ] Stroke

Gender: Male and female participants

Lower age limit: 18 Years

Upper age limit: Years

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Participants in this study are acute hospital NHS Trusts, not individual patients or clinicians.

* In England, to allow data extraction from PHE website.
* Already using the MicroGuide application for at least 12 months (to allow for capture of baseline data and adjust for seasonality).
* Demonstrating carbapenem class antimicrobial consumption within the middle band for NHS Trusts in England.
* Making antimicrobial treatment guidelines available on their hospital intranet (as an alternative to MicroGuide) for the five common infections defined above.
* Willing to replace existing guidance for the five common infections (in browse format) within the MicroGuide application with decision-support modules.
* Willing to allow organizationally identifiable data extraction from RxInfo for monthly carbapenem prescribing volumes.

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Not meeting the inclusion criteria or declining to participate.

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Gain consent from app administrators to participate.	1	0	10 minutes	Chief investigator e-mail.
App administrators to take the study proposal to an internal hospital committee for approval.	1	0	30 minutes	App administrator.
Help app administrators to iteratively develop and test DSMs based on NICE guidelines and local hospital policies, working with a local prescriber test group.	5	0	4 hours	Research fellow in person or videoconferencing.
Gain consent from app users (approximately 30 app DSM users from a subset of hospitals randomised to the intervention arm) for face-to-face interviews (or by phone or videoconferencing).	1	0	10 minutes	Research fellow by telephone.
Face-to-face interviews (on-site or by phone or videoconference) with approximately 30 app DSM users (research fellow; 45 minutes).	1	0	45 minutes	Research fellow in person or by phone or videoconferencing.

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. *These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Implementation of decision support modules (participant is the hospital)	1	N/A	1 day	Research pharmacist, working remotely

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

◉ Yes ○ No

If Yes, please give details, explain the risks and justify the need to withhold the intervention or procedure:

NHS hospital Trusts randomised to the intervention group, will have a mandatory implementation of the DSM within the Microguide app and access will be withdrawn from the standard version of the Microguide application (i.e. browse format) for the five common infections.

However, the research team will incorporate signposts within the app to direct prescribers to guideline documents hosted electronically on the hospital's intranet. Therefore the same information is available to all prescribers, but via a different route.

A21. How long do you expect each participant to be in the study in total?

All NHS hospital Trusts, in both the intervention and control arms are expected to be in the study for 12 months.

App users interviewed will be NHS Trust staff members, from Trusts randomised to DSM (intervention group). These app users will be in the study for up to one hour (consent and face-to-face interview).

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

No significant risks or burdens are anticipated as a result of participation in the proposed research.

As noted in A20, NHS Trusts randomised to the intervention group will have a mandatory implementation of the DSM within the Microguide app and access will be withdrawn from the standard version of the Microguide application (i.e. browse format) for the five common infections. It is anticipated there may be initial clinician skeptism or fear of loss of autonomy, leading to resistance and poor uptake of the DSM. This in turn could result in poor adherence to Trust's antimicrobial prescribing guidelines. To combat this risk, the research team will incorporate signposts within the app to direct prescribers to guideline documents hosted electronically on the hospital's intranet. Therefore the same information is available to all prescribers, but via a different route.

Participants in interviews will have the opportunity to share their opinions about the DSM. There is a possibility that some individuals may feel uncomfortable with revealing their personal antibiotic prescribing habits or opinions but this risk is mitigated by employing a neutral research fellow and anonymising all interview data.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

○ Yes ◉ No

A24. What is the potential for benefit to research participants?

Research participants stand to benefit from the DSM algorithms by reducing time taken on prescribing decisions and reduced risk of prescribing errors (such as allergy contra-indications) or treatment failure (if high risk of antibiotic resistance).

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? *May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.*

Following the completion of the study, the DSM will no longer be available. However NHS Trusts can continue to subscribe to the pre-existing standard 'browse' version of MicroGuide™. The DSMs will be available for a separate software licensing fee to acute hospital Trusts that wish to use this additional functionality within the MicroGuide app after the study has concluded.

A26. What are the potential risks for the researchers themselves? *(if any)*

The risks to researchers are: travel to study sites; and the remote risk of an interviewee being defensive or hostile.

Thus interviews will take place in safe environments in a convenient private space on hospital grounds and the research fellow will make contact with the chief investigator before and after each interview.

Moreover due to COVID 19 pandemic, where possible, interviews will be conducted remotely.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of social care or GP records, or review of medical records. Indicate whether this will be done by the direct care team or by researchers acting under arrangements with the responsible care organisation(s).*

Quantitative phase

Study sites will be identified from a register held by the MicroGuide App software manufacturer - Horizon Strategic Partners. A lead clinician responsible for implementation of the App (usually a specialist antibiotic pharmacist, consultant medical microbiologists or infectious diseases physicians) will be contacted by e-mail by Horizon to seek permission to be approached by the chief investigator.

As a result of the wide variation in the primary outcome variable between NHS Trusts, the study will recruit participating sites from the middle band of prescribing so as to limit variance and increase the power of the study to detect significant change.

Qualitative Phase

Staff members that have registered with Horizon Strategic Partners, have downloaded and are actively using the MicroGuide app at participating intervention hospitals will be contacted by e-mail by Horizon Strategic Partners to offer them the opportunity of participating in the interview phase of the study.

Interested individuals will contact a member of the research team, and will be sent further information about the study.

A sample of up to 30 health professionals will also be selected, comprising junior and senior doctors and nurse prescribers using the MicroGuide decision support modules for a minimum of 6 months, from the intervention group acute hospital Trusts. These individuals will be contacted and invited to take part in a semi-structured interview, expected to last for up to 45-minutes. Interviews will be conducted face-to-face or by videoconferencing.

Participants in will attend interviews in their personal time and will receive an Amazon voucher by way of reimbursement.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

○ Yes ◉ No

Please give details below:

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

Quantitative phase

Study sites will be identified from a register held by the MicroGuide App software manufacturer - Horizon Strategic Partners. A lead clinician responsible for implementation of the App (usually a specialist antibiotic pharmacist, consultant medical microbiologists or infectious diseases physicians) will be contacted by e-mail by Horizon to seek permission to be approached by the chief investigator. The chief investigator will then e-mail lead implementers at each site with an invitation to participate. Lead implementers who accept will receive a participant information sheet (PIS) and consent form by post and will be asked to sign and return via a stamped,addressed envelope when they

have had an opportunity to study the details of the PIS and consent form

Qualitative Phase

Staff members that have registered with Horizon Strategic Partners, have downloaded and are actively using the MicroGuide app at participating intervention hospitals will be contacted by e-mail by Horizon Strategic Partners to offer them the opportunity of participating in the survey and interview phase of the study.

Interested individuals will contact a member of the research team, and will be sent further information about the study, including a consent form, and will have an opportunity to study the details of the consent form.

The research fellow will contact potential face-to-face or videoconference interview participants to confirm consent and to arrange a suitable time for interview. For face-to face interviews, the research fellow will then attend the site at the agreed time, collect the signed consent form and carry out the 45-minute face-to-face interview which will be audio-recorded. For videoconference interviews, participants will be invited to confirm verbal consent and videoconference interviews will be recorded.

A30-1. Will you obtain informed consent from or on behalf of research participants?

◉ Yes ○ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

Following initial contact by the MicroGuide App software manufacturer - Horizon Strategic Partners, the chief investigator will e-mail an invitation to participate to lead implementers at each site that is willing to be contacted. Lead implementers who accept will receive a participant information sheet and consent form by post or email and will be asked to sign and return electronically or via a stamped, addressed envelope when they have had an opportunity to study the details of the consent form.

The research fellow will contact potential face-to-face or videoconference interview participants to confirm consent and to arrange a suitable time for interview. For face-to face interview, the research fellow will then attend the site at the agreed time, collect the signed consent form and carry out the 45-minute face-to-face interview which will be audio-recorded. For videoconference interviews, a participant information sheet will be provided, participants will be invited to return a a hard copy signed consent form to the research fellow and confirm verbal consent in the recorded videoconference interview.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

◉ Yes ○ No

A31. How long will you allow potential participants to decide whether or not to take part?

NHS Hospital Trust and staff members invited for interviews will be allowed two weeks to review study information and consent documents before deciding whether or not to take part

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

○ Yes

○ No

◉ Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

Recruitment is by organisation (NHS Trust) not individual patient or clinician. The senior pharmacist or clinician who represents each organization will judge whether they have capacity to participate, taking into account other concurrent or recent research activity. Use of the MicroGuide app and the decision support modules is entirely voluntary for individual clinicians. No administration of any therapeutic or prophylactic agent is required in this protocol. Individual patient consent will not be required because the study will collect and analyse aggregated outcome data and does not require individual chart review.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

All study participants will be fluent in English by virtue of their position as NHS health professional employees.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

The chief investigator will communicate via email to participating NHS Hospital Trust any amendments and updated version of research protocol, PIS and consent form.

The research fellow will communicate via email to all participating NHS staff members, any updated version of PIS and consent form.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.

○ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.

○ The participant would continue to be included in the study.

○ Not applicable – informed consent will not be sought from any participants in this research.

◉ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?*(Tick as appropriate)*

☐ Access to medical records by those outside the direct healthcare team

☐ Access to social care records by those outside the direct social care team

☑ Electronic transfer by magnetic or optical media, email or computer networks

- [ ] Sharing of personal data with other organisations
- [ ] Export of personal data outside the EEA
- [x] Use of personal addresses, postcodes, faxes, emails or telephone numbers
- [x] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals
- [x] Use of audio/visual recording devices
- [x] Storage of personal data on any of the following:
  - [x] Manual files (includes paper or film)
  - [x] NHS computers
  - [ ] Social Care Service computers
  - [ ] Home or other personal computers
  - [x] University computers
  - [ ] Private company computers
  - [x] Laptop computers

Further details:
1. Videoconference and face-to-face interviews. Digital recordings will be made of all interviews. Participants will be asked to avoid mentioning their name or place of work during the recorded interview.
2. Digital recordings and interview transcript text files will be transmitted to and from a professional transcribing company by means of a password-protected server.

A37. Please describe the physical security arrangements for storage of personal data during the study?

All data will be stored electronically in password-protected files on the servers of Portsmouth Hospitals University NHS Trust. The MicroGuide-2 researchers at the University of Portsmouth and the University of Southampton will have access to this data throughout the course of the study.

Field notes drafted by the research fellow will be pseudononymised and will be stored on the research fellow's person or in a locked university office at all times.

Any data held on laptop computers will be pseudoanonymised and only password-protected NHS laptops will be used.

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

Consenting NHS hospital Trust and participating staff members will be assigned a unique participant code number and the code-break sheet will be saved electronically as a password-protected file on the Portsmouth Hospital NHS Trust servers. The MicroGuide-2 research team at the University of Portsmouth and the University of Southampton will have access to this data throughout the course of the study. Only the chief investigator and research fellow will have access to the code-break sheet.

Videoconference and face-to-face interviews: Participants will be asked to avoid mentioning their name or place of work during the recorded interview. Digital recordings will be provided to a third-party transcription service by uploading to a password-protected server.

The research fellow will download interview transcription text files from the same password-protected server. The research fellow will assign the relevant unique participant code number to interview transcripts and will redact any text from transcripts that identifies the participant or their place of work, before analysis.

The research fellow field notes will be recorded on paper and destroyed in confidential waste once added to password-protected digital records of the interviews.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The chief investigator, principal investigators and research fellow.

Storage and use of data after the end of the study

A41. Where will the data generated by the study be analysed and by whom?

The data will be analysed on Portsmouth Hospital University NHS Trust, Universities of Portsmouth and Southampton servers by the chief investigator, principal investigators and the research fellow.

A42. Who will have control of and act as the custodian for the data generated by the study?

	Title	Forename/Initials	Surname
	Miss	Adefunke	Bamgboye
Post	Reserach Pharmacist		
Qualifications	PgCert Pharmacy practice MPharm (Pharmacy)		
Work Address	Pharmacy Research Office		
	Portsmouth Hospitals University NHS Trust		
	C level Queen Alexandra Hospital		
Post Code	PO6 3LY		
Work Email	adefunke.bamgboye@porthosp.nhs.uk		
Work Telephone	(023) 9228 6000		
Fax			

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ○ 6 – 12 months
- ○ 12 months – 3 years
- ◉ Over 3 years

If longer than 12 months, please justify:
Source data will be retained by Portsmouth Hospitals University NHS Trust for 10 years from the end of the study period, which is a standard requirement of the collaborating University of Southampton. It will be anonymised.

A44. For how long will you store research data generated by the study?

Years: 10
Months:

A45. Please give details of the long term arrangements for storage of research data after the study has ended. *Say where data will be stored, who will have access and the arrangements to ensure security.*

Data will be archived securely in password-protected files on Portsmouth Hospitals University NHS Trust servers. Passwords will be held by the research and innovation office at Portsmouth Hospital University NHS Trust.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

(●) Yes ( ) No

If Yes, please give details. For monetary payments, indicate how much and on what basis this has been determined.
Free-of-charge system access to MicroGuide™ decision support modules for the full 12-month duration of the study will be given to participating NHS Trusts.

Participants in 45-minute face-to-face interviews will receive a £30 Amazon voucher.

The payments have been determined on the basis of market rates for locum healthcare staff.

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

( ) Yes (●) No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

( ) Yes (●) No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

( ) Yes (●) No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

PUBLICATION AND DISSEMINATION

A50-1. Will the research be registered on a public database?

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

(●) Yes ( ) No

Please give details, or justify if not registering the research.
The study protocol will be registered with clinicaltrials.gov and researchregistry.com

Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

- [x] Peer reviewed scientific journals
- [x] Internal report
- [x] Conference presentation
- [ ] Publication on website
- [ ] Other publication
- [ ] Submission to regulatory authorities
- [ ] Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- [ ] No plans to report or disseminate the results
- [ ] Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

N/A

A53. How and when will you inform participants of the study results?

If there will be no arrangements in place to inform participants please justify this.
Summary report and copies of published papers will be provided to all participating sites.

5. Scientific and Statistical Review

A54-1. How has the scientific quality of the research been assessed?*Tick as appropriate:*

- [ ] Independent external review
- [x] Review within a company
- [ ] Review within a multi−centre research group
- [x] Review within the Chief Investigator's institution or host organisation
- [ ] Review within the research team
- [ ] Review by educational supervisor
- [ ] Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
The protocol was reviewed by the multi-disciplinary project team and the completed protocol was subsequently submitted to Merck Sharp and Dohme (MSD) for internal scrutiny and the protocol was refined in light of feedback from company reviewers (approval document attached).

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed?*Tick as appropriate:*

- [ ] Review by independent statistician commissioned by funder or sponsor
- [ ] Other review by independent statistician
- [ ] Review by company statistician
- [x] Review by a statistician within the Chief Investigator’s institution

☐ Review by a statistician within the research team or multi−centre group

☐ Review by educational supervisor

☐ Other review by individual with relevant statistical expertise

☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Dr	Ngianga	Kandala
Department	Faculty of Science and Health, School of Health and Care Professions		
Institution	University of Portsmouth		
Work Address	Rosalind Franklin West		
	White Swan Road		
	Portsmouth		
Post Code	PO1 2DT		
Telephone	02392842847		
Fax			
Mobile			
E-mail	ngianga.kandala@port.ac.uk		

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Carbapenem prescribing volume measured as Defined Daily Doses (DDD) per thousand admissions per NHS Trust aggregated at hospital Trust level.

A58. What are the secondary outcome measures?*(if any)*

a. Piperacillin-tazobactam prescribing volume measured as DDD per thousand admissions per NHS Trust aggregated at hospital Trust level.
b. Antimicrobial resistance rates (E. coli resistance to piperacillin-tazobactam).
c. MicroGuide software usage levels and patterns of use.
d. Aggregate outcome data for adult inpatients with coded diagnosis of any of the infections covered by the decision support modules: length-of-stay, 30-day readmission, ICU admission and in-hospital mortality.

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:	24
Total international sample size (including UK):	24
Total in European Economic Area:	24

Further details:
The sample size represents 24 NHS hospital Trusts. This includes 12 NHS Trusts per randomised arm.

For interviews with staff members, a sample size of 30 has been selected.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

For the primary outcome, the sample size is based on middle band carbapenem prescribing volumes at baseline, the

study will have 80% power (α=0.05) to detect a change of 15% in the primary outcome with 9 NHS Trusts per arm, or 90% power (α=0.05) with 12 NHS Trusts per arm

For interviews, the sample size of 30 for interviews was selected based on experience from the MicroGuide-1 study that saturation of interview themes was achieved following interview of this number of participants. This sample size allows for at participants from each NHS Trust in the intervention arm to be represented.

We will also use an interview sampling framework to ensure adequate representation of junior and senior doctors as well as nurse prescribers.

A61-1. Will participants be allocated to groups at random?

(●) Yes ( ) No

If yes, please give details of the intended method of randomisation:
Two-arm parallel randomized
Sites will be randomised using the Sealed Envelope online tool (https://www.sealedenvelope.com/randomisation/).

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

QUANTITATIVE DATA ANALYSIS

The primary quantitative outcome will be analysed by independent t-test of intervention against control arms, using monthly carbapenem prescribing data from July 2021 to June 2022.

Secondary quantitative outcomes (a) and (b) will use the same method as the primary outcome.

Tertiary outcomes will use the same method as the primary outcome or the Mann-Whitney U Test dependent upon the distribution of the variable.

All quantitative outcome variables will be analysed independently using aggregated hospital-level data and it will not be possible, nor any attempt made, to link prescribing and clinical outcome data at the individual patient level. Secondary quantitative outcome (c) will be analysed by descriptive and exploratory statistics.

QUALITATIVE DATA ANALYSIS

Interview data will be analysed using a thematic analysis process. Interview data will be transcribed by University-approved independent transcription services, who will store and manage data in accordance with our ethical approval and University regulations. This will include anonymising any identifiable data in audiorecordings during transcription. Thematic analysis of data will take place at the researcher's place of employment and Portsmouth Hospitals University NHS Trust. Anonymised data will be shared with the Universities of Southampton and Portsmouth for the process of data analysis. Transcripts will be transferred via
encrypted secure software. NVivo qualitative data management software will be used to help manage the data.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Dr	Kieran	Hand
Post	National Pharmacy & Prescribing Clinical Lead - antimicrobial resistance		
Qualifications	PhD, MSc, BSc		
Employer	NHS England		
Work Address	Skipton House		
	80 London Road		

	London
Post Code	SE1 6LH
Telephone	
Fax	
Mobile	
Work Email	kieran.hand@nhs.net

Title	Forename/Initials	Surname
Dr	Kordo	Saeed

Post	Consultant Clinical Microbiologist
Qualifications	MB ChB MSc FRCPath MD
Employer	University Hospital Southampton NHS Foundation Trust
Work Address	Southampton General Hospital
	Tremona Road
	Southampton
Post Code	SO16 6YD
Telephone	
Fax	
Mobile	
Work Email	kordosaeed@nhs.net

Title	Forename/Initials	Surname
Prof	Sue	Latter

Post	Professor of Health Services Research
Qualifications	PhD, BSc(Hons) RN, PGDipHV
Employer	School of Health Sciences, University of Southampton
Work Address	Room number: 67/4065
	Highfield
	Southampton
Post Code	SO17 1BJ
Telephone	(023) 8059 7959
Fax	
Mobile	
Work Email	S.M.Latter@soton.ac.uk

Title	Forename/Initials	Surname
Miss	Adefunke	Bamgboye

Post	Research Pharmacist
Qualifications	MPharm, pgCert
Employer	Portsmouth Hospitals University NHS Trust
Work Address	Queen Alexandra Hospital
	Pharmacy Department C Level research office, Queen Alexandra Hospital
	Southwick Hill Road, Portsmouth
Post Code	PO6 3LY
Telephone	02392 286000 Ext 6867
Fax	
Mobile	
Work Email	adefunke.bamgoye@porthosp.nhs.uk

	Title	Forename/Initials	Surname
	Ms	Anisha	Soni
Post	Chief Pharmaceutical Officer's Clinical Fellow		
Qualifications	MParm, MSc, pgDip, CIPPET		
Employer	NHS Engalnd		
Work Address	Skipton House 80 London Road London		
Post Code	SE1 6LH		
Telephone			
Fax			
Mobile	07730 375410		
Work Email	anisha.soni@nhs.net		

	Title	Forename/Initials	Surname
	Dr	Mike	Allen
Post	Regional Medical Advisor		
Qualifications	BSc, DPhil		
Employer	Merck Sharp & Dohme (UK) Ltd		
Work Address	120 Moorgate London		
Post Code	EC2M 6UR		
Telephone			
Fax			
Mobile	07779 706336		
Work Email	mike.allen@msd.com		

	Title	Forename/Initials	Surname
	Mrs	Amazigom	Mayes
Post	Senior HTA & EBM Manager		
Qualifications	BSc (Hons), MSc		
Employer	Merck Sharp & Dohme (UK) Ltd		
Work Address	120 Moorgate London		
Post Code	EC2M 6UR		
Telephone			
Fax			
Mobile	07974 444655		
Work Email	amazigom.okafor@msd.com		

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status: ○ NHS or HSC care organisation

Commercial status: Commercial

- ○ Academic
- ◉ Pharmaceutical industry
- ○ Medical device industry
- ○ Local Authority
- ○ Other social care provider (including voluntary sector or private organisation)
- ○ Other

If Other, please specify:

Contact person

Name of organisation	MERCK SHARP & DOHME (UK) LIMITED
Given name	Mike
Family name	Allen
Address	120 Moorgate
Town/city	London
Post code	EC2M 6UR
Country	United Kingdom
Telephone	07779 706336
Fax	
E-mail	mike.allen@msd.com

Legal representative for clinical investigation of medical device (studies involving Northern Ireland only)
Clinical Investigations of Medical Devices that take place in Northern Ireland must have a legal representative of the sponsor that is based in Northern Ireland or the EU

Contact person

Name of organisation	
Given name	
Family name	
Address	
Town/city	
Post code	
Country	
Telephone	
Fax	
E-mail	

A65. Has external funding for the research been secured?

Please tick at least one check box.

- ☑ Funding secured from one or more funders
- ☐ External funding application to one or more funders in progress

☐ No application for external funding will be made

What type of research project is this?

◉ Standalone project
◯ Project that is part of a programme grant
◯ Project that is part of a Centre grant
◯ Project that is part of a fellowship/ personal award/ research training award
◯ Other

Other – please state:

Please give details of funding applications.

Organisation	MERCK SHARP & DOHME (UK) LIMITED
Address	120 Moorgate
	London
	United Kingdom
Post Code	EC2M 6UR
Telephone	
Fax	
Mobile	
Email	edita.custic@msd.com

Funding Application Status: ◉ Secured ◯ In progress

Amount: £201,628

Duration
Years: 2
Months: 6

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?

The Sponsor (MSD UK – also known as Merck & Co in the USA and Canada) is the sole funder of this project and the funding is independent of MSD products.

MSD is one of the founding board members of the AMR Industry Alliance and committed to advancing antimicrobial stewardship to improve patient outcomes, slow the development of AMR and supporting global AMR surveillance.

MSD does not have any commercial relationship with Horizon SP.

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? *Please give details of subcontractors if applicable.*

◯ Yes ◉ No

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

◯ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title	Forename/Initials	Surname
	Ms	Antonia	Baker
Organisation	Portsmouth Hospitals University NHS Trust		
Address	Research Department, 1st Floor, Lancaster House		
	Queen Alexandra Hospital		
	Cosham Portsmouth		
Post Code	PO6 3LY		
Work Email	Antonia.Baker@porthosp.nhs.uk		
Telephone	02392 286000		
Fax			
Mobile			

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A68-2. Select Local Clinical Research Network for NHS Organisation identified in A68-1:

Wessex

For more information, please refer to the question specific guidance.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 15/09/2021
Planned end date: 14/04/2023
Total duration:
Years: 1 Months: 6 Days: 0

A71-1. Is this study?

- ○ Single centre
- ◉ Multicentre

A71-2. Where will the research take place? *(Tick as appropriate)*

- ☑ England
- ☐ Scotland
- ☐ Wales
- ☐ Northern Ireland
- ☐ Other countries in European Economic Area

Total UK sites in study 24

Does this trial involve countries outside the EU?

(●) Yes ( ) No

[ ] USA

[x] Other international (please specify)

England

A72. Which organisations in the UK will host the research? *Please indicate the type of organisation by ticking the box and give approximate numbers if known:*

[x] NHS organisations in England	24
[ ] NHS organisations in Wales	
[ ] NHS organisations in Scotland	
[ ] HSC organisations in Northern Ireland	
[ ] GP practices in England	
[ ] GP practices in Wales	
[ ] GP practices in Scotland	
[ ] GP practices in Northern Ireland	
[ ] Joint health and social care agencies (eg community mental health teams)	
[ ] Local authorities	
[ ] Phase 1 trial units	
[ ] Prison establishments	
[ ] Probation areas	
[ ] Independent (private or voluntary sector) organisations	
[ ] Educational establishments	
[ ] Independent research units	
[ ] Other (give details)	
Total UK sites in study:	24

A73-1. Will potential participants be identified through any organisations other than the research sites listed above?

(●) Yes ( ) No

A73-2. If yes, will any of these organisations be NHS organisations?

( ) Yes (●) No

If yes, details should be given in Part C.

A74. What arrangements are in place for monitoring and auditing the conduct of the research?

Monitoring of the study will be carried out at monthly intervals by means of teleconferences with the study sponsor, Merck Sharp & Dohme (UK) Ltd. Auditing of the conduct of this research will be carried out according to the policies of Merck Sharp & Dohme (UK) Ltd.

An advisory group will be set up, comprising NHS clinicians, pharmacist prescribers and nurse prescribers.

A75-1. What arrangements will be made to review interim safety and efficacy data from the trial? Will a formal data monitoring committee or equivalent body be convened?

N/A

If a formal DMC is to be convened, please forward details of the membership and standard operating procedures to the Research Ethics Committee when available. The REC should also be notified of DMC recommendations and receive summary reports of interim analyses.

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

1. Errors detected in how the app executes the decision support logic.
2. Negligible adoption of the decision support modules despite repeated efforts.
3. Insufficient sites recruited to power the study adequately.
4. Commercial issues with the app supplier.
5. Regulatory changes impacting the use of the decision support modules.
6. Withdrawal of funding by the sponsor.

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:** in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland*

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (NHS sponsors only)

☑ Other insurance or indemnity arrangements will apply (give details below)

Casualty Policy, policy number UKCANC48823, issued by ACE European Group Limited, London, in the name of Merck Sharp & Dohme (UK) Ltd

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

☑ NHS indemnity scheme will apply (protocol authors with NHS contracts only)

☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional

indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

☑ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

○ Yes ◉ No

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

○ Yes ○ No ◉ Not sure

Part B: Section 2

A. General information

Information in this sub-section will be included in applications to the Research Ethics Committee and NHS R & D offices at the research sites.

1. Is the manufacturer (or other organisation responsible for developing the device) the same organisation named as lead sponsor for this study?

○ Yes ◉ No

If No, please give details of the manufacturer or other organisation responsible for developing the device below:

Organisation Each intervention site will develop its own decision support modules
Address

Post Code
Country
Telephone
Fax
Mobile
E-mail

2. Details of the medical devices to be used in the study

Name of the manufacturer: Each intervention site

Manufacturer's trade name for the device:	Antimicrobial Decision Support Modules (DSMs)
Device identification name and/or number:	
Name:	DSM
Number:	001-005
Generic name of device and principal intended use(s):	DSMs for community-acquired pneumonia and hospital-acquired pneumonia, urinary tract infection, cellulitis, and biliary tract infection. The project team will work with each participating site in the intervention arm to help them develop a DSM based on NICE guidelines and adapted to local hospital policies and pharmacy purchasing arrangements. Each site will test and sign-off their DSMs before they are implemented in the MicroGuide app. Each site will have a unique PIN so that access to the DSMs is limited to the site that developed them.
Length of time since device came into use:	DSMs are being created as part of this study.

3-1. Further details of the purpose of the study

Does the study involve:

- (●) Investigation of a new medical device
- ( ) Investigation of new implantable material
- ( ) Use of an existing product outside the terms of its UKCA/CE UKNI/CE marked intended purpose
- ( ) Use of a modified product
- ( ) Use of an existing product within its UKCA/CE UKNI/CE marked intended purpose

3-2. Please give further details below including the following:

Description of any new device, materials, method of use or operation with a summary of the intended purpose.

The basic MicroGuide app offers prescribers easy access to antimicrobial guidelines for quick reference, but it does not offer structured decision support based on specific patient details. MicroGuide offers the functionality for acute hospital Trusts to create decision support modules (DSMs) for particular conditions, so that prescribers can answer a series of conditional questions about factors such as disease severity, allergies, resistance risks and pregnancy status to be guided to a recommended choice of drugs or in some cases to seek further microbiology specialist advice. The DSMs are predicated on the content of existing local prescribing guidelines in each acute hospital Trust and simply re-frame the guideline content into a decision-support algorithm

Composition of any new implantable materials, including summary of biocompatibility findings from studies to date.

N/A

A summary of any modifications to UKCA/CE UKNI/CE marked devices.

A summary of any proposed changes to the UKCA/CE UKNI/CE marked intended purpose.

For all products with UKCA/CE UKNI/CE mark please attach instructions for use.

9. Has the study been the subject of a scientific review/opinion (Expert Panel)?

( ) Yes (●) No

If yes, please provide a copy of the review as part of your application.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For further information please refer to guidance.*

Investigator identifier	Research site	Investigator Name	
IN4	(●) NHS/HSC Site ( ) Non-NHS/HSC Site Organisation name Address Post Code Country	Forename Middle name Family name Email Qualification (MD...) Country	Sites will be recruited and confirmed following a favourable ethics opinion and HRA approval, and submitted as a minor amendment.