PIPP-1122-G – ANNEX B

REVIEW OF EMGERENCY PREPAREDNESS AND CLINICAL COUNTERMEASURES: FORMAL ADVISORY PHASE RECOMMENDATIONS

1. This paper provides an overview of all the recommendations provided as part of the Formal Advisory Phase of the Review of Emergency Preparedness and Clinical Countermeasures.

Governance and Management recommendations

Service Delivery Roles and Responsibilities

2. It is the recommendation of UKHSA VCR and SCCL, as the management function of the NHSSC, that:
    a. UKHSA VCR team continues to be responsible for:
        i. Advanced Purchase Agreement (APA) for Pandemic Specific (Influenza) Vaccine (PSV)
        ii. All Pharmaceutical products associated with future pandemic preparedness requirement for PIPP (and EPRR)
        iii. COVID medicines
        iv. All consumables associated with the administration of the above pharmaceuticals including combined needles and syringes for administration of the PSV.
    b. SCCL (through the NHSSC) takes over the responsibility for:
        i. Implementing the defined strategy for PPE and related consumables (including infection control products) for Pandemic Preparedness. This would include developing category strategies that can deliver the defined PPE strategy. This is in addition to continued responsibility for these products in Business as Usual (BAU).
        ii. Subject to the requirements of the defined strategy (currently under development), transfer of remaining volumes of PPE consumables that UKHSA were responsible for procuring during COVID-19, specifically the Powered Hood Filters, to ensure this asset can be drawn down upon by trusts as needed in future pandemics.

Deployment decision-making framework for pandemics and high-consequence infectious diseases

3. Considerations for the deployment and response structures that are stood up in a response are highly dependent on the type of incident. Below is a table outlining the recommendations of the governance subgroup on deployment of response:

Issue	Pandemics	HCID and emerging infectious disease cases or outbreaks
Structures	• Decision making regarding clinical countermeasures in a pandemic should be integrated into the incident response structures established at the time. It is expected that UKHSA would establish, lead, and run these initially, but this may change over the course of a pandemic. • UKHSA-led specific countermeasure cells (e.g. PPE, vaccine, medicines) with assigned leads should be set up very early in the response (possibly before first UK cases) given lead-in times to deployment. • The cells should have responsibility for developing deployment strategies based on clinical and scientific advice; advising on when and how to deploy stockpiles; longer-term procurement and deployment strategies beyond the initial stockpile use; management of procurement, storage, and deployment; and all related policy functions.	• An UKHSA-led incident response structure will be set up in HCID cases. • For small incidents, there is unlikely to be a need for sub-cells. In larger, ongoing outbreaks, specific countermeasure cells with assigned leads should be set up by UKHSA with the same responsibilities as in a pandemic.
Decision-making authority	• Decisions on deployment of stockpiled products should be made by SofS or delegated ministers, following cell advice.	• HCID cases require an immediate deployment of stock. The deployment strategy for these clinical countermeasures should have been developed in advance, and in most HCID incidents will only be for use in a small, limited number of individuals. As such, the decision and authority to deploy should rest with the incident director. • In some cases (e.g. monkeypox), the incident may develop into a larger, more prolonged outbreak and a revised deployment strategy on a larger scale may need to be implemented. Significant changes to deployment strategies and large-scale deployment from stockpiles should be agreed with SofS or ministers following advice from relevant cells.
Deployment strategies	• Cells should develop deployment strategies (i.e. eligibility/prioritisation for vaccination, number of doses, etc.) with advice from expert advisory committees, UKHSA clinical and public health advice, and CMO/DCMO advice. • Deployment strategies should include whether any products will be subject to trials to determine efficacy.	• For small HCID incidents, how clinical countermeasures will be deployed should have been agreed in advance. For larger outbreaks, new deployment strategies may need to be developed in the same way as in a pandemic.

	• The overall response structure should include processes and structures for commissioning and coordinating scientific advice to avoid duplication or confusion in scientific advice.	
Four nations coordination	• Deployment of respective stocks is a decision reserved for each nation, but if desired mechanisms should be developed for receiving joint advice and coordinating on development of deployment strategies; and coordinating on procurement. • The pandemic-specific vaccine advance purchase agreement (APA) is, however, a single contract and so decisions for its activation should be made jointly.	• HCID cases tend to be highly localised. • Stocks will differ in whether they are held in a single central stockpile or distributed across the four nations, and whether there are pre-assigned volumes owned by/designated for each nation. • If stocks are assigned to specific nations, stock deployment should be decided within their own response structures which will have been stood up. • If stocks are not pre-assigned, deployment will need to be agreed with the assigned responsible UKHSA lead; but this should be agreed rapidly and without issue if the requests is in line with pre-agreed deployment strategy.

4. In discussion, the Governance and Management subgroup also advised that the framework for describing different phases of a pandemic (e.g. the WHO pandemic influenza phases) currently used for guiding the UK response, should be reconsidered in light of COVID-19.

Coordination of countermeasures across the four UK nations, Overseas Territories (OT) and Crown Dependencies (CD)

5. It was agreed to re-affirm a continuation of the current arrangements for coordination amongst the four nations on pandemic countermeasures.
6. Noting that the Scottish Government is exploring its own procurement routes for PPE, the four UK nations should continue to coordinate on the planning assumptions underpinning this, i.e. on the specific PPE products and volumes held for different risks.
7. Noting the potential for HCID countermeasure arrangements to be made in future:
    i. HCID and other emerging infectious disease risks and the products and volumes held in response to those risks are agreed on a four nation basis
    ii. The management, storage, and financing models for specialised stockpiles should be agreed on a case-by-case basis according to requirements, given the different operational parameters for HCID versus pandemic stockpile and response. These options may include a single stockpile covering all four nations, and volume allocations and funding contributions that do not follow the Barnett formula.
8. The subgroup did not make any definitive recommendations as to OTs and CDs inclusion or exclusion from future arrangements; but recommended that further

conversations are held to explore the possibility of including OTs and CDs in countermeasures preparedness arrangements in future.

Future clinical countermeasures governance

9. In future, it is recommended that the pandemic preparedness clinical countermeasures programme include a research, capability, and industry engagement coordination group.

10. The Clinical Countermeasures Board (CCMB) should continue operating with its existing remit with UKHSA in the chair, covering the clinical countermeasure UK stockpiles and the agreements required to ensure that the UK is well prepared to respond effectively to a pandemic.

    a. future scope includes any stockpiles and related agreements developed for other pandemic, emerging infectious disease or HCID risks (e.g. Imvanex); and the National Pandemic 'Flu Service (NPFS).

    b. meetings move to quarterly (from bi-annually).

    c. UKHSA should update the terms of reference to reflect these changes; and the membership as appropriate.

11. CCMB will continue to report into every meeting of PIPP on England stockpiles and provide high-level updates including an assessment of overall delivery confidence on delivery of PIPP stockpile targets. All significant risks or issues should be presented to PIPP, including escalation of decisions as appropriate.

12. Workstreams relating to clinical countermeasures that fall outside of the scope of the CCMB (i.e. relating to development or review of policy or scientific advice) shall be agreed by the PIPP Board or PIPP Senior Responsible Officer (SRO), captured in the PIPP work programme, and sit directly under and report to the PIPP Board. If a workstream is significant enough, then an additional governance sub-structure or process may be put in place beneath PIPP to manage the work.

13. The PIPP Board is expected to commission a cross-system review of clinical countermeasures approximately every 3-5 years to ensure the approach remains fit for purpose and aligned with wider government and sector activity.

14. Policy development and reviews shall be led by the lead policy team in collaboration with colleagues on the CCMB. While not members of the PIPP Board, Devolved Governments should be engaged in this work on the basis that clinical countermeasures are an area where the four nations aim to coordinate. Following agreement of any new clinical countermeasures policy or changes to existing policy by ministers, its operationalisation shall fall under the CCMB.

15. Deployment of countermeasures shall be governed separately under incident and emergency response structures, as outlined above.

16. Preparation of Spending Review bids should be led by the responsible policy teams, working with other members of the CCMB.

PPE recommendations

17. PPE subgroup members recommended the below PPE ensemble for pandemic preparedness stockpiles, which would be effective against a novel respiratory pathogen. Advisory Board members approved the below recommended PPE.

PPE item	Usage information
FFP3 respirator (non-valved)	• Sessional usage, including entry into cohorted areas • Replace when visibly damaged and/or contaminated • Use in conjunction with face shield to extend usable life
Gloves	• Single pair per patient or replace when visibly damaged
Gown (full body)	• For use where risk of aerosol spread and/or splash risk. **Mandatory** for Aerosol Generating Procedures (AGP).
Splash-proof apron (dispensing option dependent on setting)	• Default torso/body protection usage, unless enhanced protection needed where risk present *(swap for full body gown if this is the case)*
Face shield/visor	• Sessional use default unless demand is high and manufacturer specification allows for disinfection/usage in this way.

18. This ensemble marks a significant departure from previous pandemic influenza guidance, with the newly proposed ensemble recommending an FFP3-grade respirator in all scenarios (compared to being reserved for aerosol generating procedures (AGPs) in the previous guidance). The respirator is to be worn during all procedures or contact with potentially infected individuals, and eye protection is to be used for all procedures, not just in AGPs.

Medicines recommendations

19. The medicines subgroup recommended the following advice on medicines to stockpile, or to consider for stockpiling. Advisory Board members approved the below recommendations.

Pandemic Response: MHRA Licensed medicines and vaccines recommended for stockpiling

20. Influenza antivirals:

"Driver"[1] pathogen	Medicine	Recommendation
Pandemic influenza	**Oseltamivir**	To be held as the primary antiviral for an influenza pandemic.
Pandemic influenza	**Irrelevant & Sensitive**	To be held in the strategic reserve, quantities and presentations dependent on the **Irrelevant & Sensitive** to the PIPP stockpile programme.
Pandemic influenza		**I&S** **I&S**, should form the basis of the strategic reserve of alternative antivirals.

[1] The "Driver" pathogen is the pathogen that forms the main justification to hold the medicine and the basis of the RWCS to be used to calculate requirements.

21. **COVID-19 antivirals** to be considered following step-down of the current pandemic response:

"Driver" pathogen	Medicine	Recommendation
SARS-CoV-2	**Molnupiravir**	Future stockpiling requirements to be informed by learning from COVID-19 pandemic and Reasonable Worst-Case Scenario (RWCS) for a future coronavirus pandemic with limited and/or no population immunity and/or vaccine.
SARS-CoV-2	**Paxlovid**	

22. **Antibiotics for a respiratory pandemic**:

"Driver" pathogen	Medicine	Recommendation
Pandemic influenza	**Co-amoxiclav**	To be held in a range of presentations to treat bacterial complications of influenza in both primary and secondary care settings.
Pandemic influenza	**Doxycycline**	
Pandemic influenza	**Clarithromycin**	
Pandemic influenza	**Cefuroxime**	To be held in an IV infusion format to treat bacterial complications of influenza in secondary care settings.

23. The antibiotic amoxicillin is <u>not recommended</u> for stockpiling as it has less effect upon Staphylococcus aureus which is a recognised cause of influenza-related bacterial pneumonia. Amoxicillin is <u>not to be used as a substitute</u> for the antibiotic medicines listed above.

<u>Supportive medicines</u>

24. Medicines to support the continued provision of ITU services during a pandemic should therefore be stockpiled:

Type	Medicine	Recommendation
Opioid	**I&S**	These medicines should be held to mitigate supply chain issues and maintain ITU provision during a RWCS scale Pandemic. Quantities held should be proportionate to requirements of the RWCS and reflect the resilience of the 'business as usual' supply chain (i.e., the level of supplies that can be maintained in a pandemic situation).
Opioid		
NMBAs		
Neuromuscular Blocking Agent		
Neuromuscular Blocking Agent		

Vasopressors and inotropes	I&S	
Vasopressors and inotropes		
Sedatives		
Sedatives		
Antipyretics		
Thromboprophylaxis/ Anticoagulation		
Electrolytes		
Antibiotic		

25. Additionally, the Medicines Subgroup noted that:

    a. advice on Pandemic Specific Vaccines (PSV) for influenza had already been provided (jointly) by JCVI and NERVTAG and accepted by the previous Secretary of State (SofS)

    b. further advice has been commissioned from NERVTAG on the possible use of influenza antivirals for pre-exposure prophylaxis

    c. NERVTAG and JCVI, as part of this exercise, are jointly considering advice relating to the stockpiling and use of Pre-Pandemic Vaccines (PPV) for influenza.

HCID Response: MHRA Licensed medicines and vaccines recommended for stockpiling

26. The following licenced medicines and vaccines should be stockpiled, or other arrangements for access be made, to support a response to outbreaks of High Consequence Infectious Disease (HCID):

"Driver" pathogen	**Medicine**	**Purpose**	**Recommendation**
Zoonotic influenza	Oseltamivir (oral)	Treatment and Post-Exposure Prophylaxis	Should be stockpiled to respond to zoonotic influenza, both local outbreaks and RWCS events. Anticipated to be available from pandemic stockpiles if required
Zoonotic influenza	I&S	Treatment and Post-Exposure Prophylaxis	
Zoonotic influenza		Treatment and Post-Exposure Prophylaxis	I&S

I&S is not interchangeable with other antibiotics held to respond to a respiratory pandemic and/or secondary complications of influenza.

Monkeypox	**I&S**	Should be stockpiled in sufficient quantities to respond to a RWCS scale monkeypox outbreak caused by a more serious clade of the virus than is currently circulating in the UK and globally.
Monkeypox		Should be stockpiled in sufficient quantities **I&S** line with scientific/clinical advice received in a future RWCS scale monkeypox outbreak caused by a more serious clade of the virus.

27. **I&S**

HCID Response: Unlicensed medicines and those used off-licence for consideration in any prioritisation and stockpiling exercise

28. It is recommended that in addition to stockpiling of licenced products, there should also be stockpiles of limited quantities of unlicenced medicines and medicines to be used off-licence. These fall into two groups: monoclonal antibodies and antivirals.

29. For Monoclonal antibodies, a mixture of Just-in-case (JIC) and Just-in-Time (JIT) stockpiling was felt to be most appropriate given the nature of the pathogens and medicines. Two such drugs are recommended at this time, with others in development.

"Driver" pathogen	**Medicine**	**Purpose**	**Recommendation**
Ebola – Zaire strain	Inmazeb (cocktail of 3 monoclonals)	Treatment (secondary care)	Monoclonal antibodies are recommended as the preferred treatment for Ebola (Zaire strain) by the Subgroup and the WHO. Initially DHSC should look at procurement of sufficient quantities to treat a small number of imported cases (i.e., no-notice cases within the RWCS). With regards wider stockholding, DHSC should consider investing in an ability to manufacture and/or procure monoclonals

Ebola – Zaire strain	Ebanga (single monoclonal)	Treatment (secondary care)	after they are shown to work during a viral haemorrhagic fever outbreak as an alternative to large scale stockpiling.

30. For antiviral medicines, the Medicines Subgroup recommended limited stockholdings of a range of drugs that might have efficacy. The limited human data for these medicines means the evidence to support large scale stockpiling does not exist. However, stockpiling limited amounts to create a "library" of medicines and using them on an "experimental basis" could potentially develop the evidence for later stockpiling if cases were to occur.

31. The limited stock could be partially pre-deployed into the NHS and might also provide a range of options for possible treatments if viruses where little research had taken place were to be imported into the UK (e.g. Ebola – Sudan strain):

"Driver" pathogen	**Medicine**	**Purpose**	**Possibly effective against**	**Recommendation**
Lassa Fever	**I&S**	Treatment (secondary care)	MERS, SARS, and CCHF	Should be stockpiled in small quantities to create a "library" of antivirals to support treatment of limited numbers of imported and/or no-notice cases of a range of pathogens. Stockpiles should, where possible be pre-deployed into appropriate NHS HCID Units to support required speed of access. Consideration should be given to the necessary paperwork and regulatory approvals if these are to be held on an "experimental" basis.
Marburg Virus		Treatment (secondary care)	Nipah Virus	
Middle East Respiratory Syndrome (MERS)		Treatment (secondary care)	N/A	
Marburg Virus		Treatment and Post-exposure prophylaxis (secondary care)	CCHF	
Ebola – Zaire strain		Treatment (secondary care)	Marburg Virus	
Monkeypox		Treatment (secondary care)	Other uses not within the scope of the Medicines Subgroup	
Monkeypox		Treatment (secondary care)		
Monkeypox		Treatment (secondary care)		

32. For these antiviral medicines, it is recommended that a separate **prioritisation exercise** is undertaken to determine which should be held. This exercise should consider the risk to the UK; availability of medicines; potential use of each medicine against a range of pathogens; cost-effectiveness; and other benefits in holding these medicines to mitigate risks not within the scope of Medicines Subgroup discussions.

33. It will be important to regularly review these stockpile recommendations as knowledge of HCID treatments evolve and new medicines are developed.

Medical Consumables

34. Medical consumables were not directly considered under the Review. Instead, consumables associated with the delivery of medicines (needles, syringes, sharps bins etc.) will be considered during the implementation phase of the project as the final decision on medicines to hold and/or contract for (e.g. the APA for pandemic influenza) will inform the materials needed to deliver those medicines. Furthermore, consideration of the resilience of the UK supply chain in a RWCS scale pandemic will need to be taken into account when considering requirements.

Hygiene Consumables

35. IPC Cell Colleagues provided the below initial recommendations on hygiene consumables that should form part of the pandemic preparedness stockpiles.

Item	Narrative	Pandemic and/or HCID stockpile
Environmental Cleaner (covering detergent and disinfectant)	Detergent and disinfectant. A combined product may be most suitable. Hypochlorite would be most resilient as all infectious agents are susceptible to this.	Both
Single use wipes	Consideration should possibly be given to disposable wipes for equipment decontamination; these would be required to be effective against the relevant infectious agents.	Both
Liquid Soap (non-antimicrobial and antimicrobial)	**Non-antimicrobial liquid soap:** Recommended for use when hands are visibly contaminated/soiled (with dirt, blood, body fluids) or when there is likely to be exposure to spore forming organisms (e.g. C. difficile, Bacillus anthracis) or gastrointestinal (GI) infections (e.g. norovirus). **Antimicrobial liquid soap:** Recommended when carrying out WHO hand hygiene moment 2, i.e. before a clean/aseptic procedure, for surgical hand antisepsis, and its use has been suggested in areas where high risk patients are cared for during outbreaks.	Both

Alcohol based hand rub (ABHR)	ABHR solutions containing 62-90% alcohol by volume is the preferred product for hand hygiene in health and care settings	Both
Clinical waste bags	Type/Colour TBC	Both
Reusable cloths	May need to understand demand / learning from COVID-19	Both
Reusable mop heads	May need to understand demand / learning from COVID-19	Both
Gelling agents	Gelling agents if liquid waste cannot be disposed into sewerage/sluice?	HCID
Alginate Bags	Alginate bags for increased volume of infectious linen?	HCID
Rigid containers (for clinical waste)		HCID

36. Paper Towels are not included within the initial stockpiling advice for the pandemic RWCS due to low demand during the COVID-19 pandemic, which was met by the business as usual (BAU) supply chain.

Research and Development

Gaps in knowledge underpinning RWCS

37. Areas for potential further research were divided into:

    d. Areas where further information needs to be generated to support the development of specific RWCSs

    e. Areas where the further research is required to support the use of scenarios in the development and testing of new pandemic plans and policies.

38. Specific research recommendation areas are as follows:

Topic area	**Recommendation**
Spontaneous behavioural change	Spontaneous population behaviour change means a truly unmitigated RWCS is considered unlikely. Further research is needed to understand the impact spontaneous behavioural change could have on the course of a pandemic and to support the testing of policy options.
Vector Borne Disease (VBD)	Research/literature review into possible longer-term trends in risk of VBD outbreaks linked to environmental changes. This would inform the development of more accurate projection of, and scenarios for, longer term risks.
VBD	Research/literature review into which imported pathogens could be spread by insect vectors (e.g. midges) already present in the UK. This would inform the development of more accurate scenarios and risk assessments.

Containment	Research on the effectiveness and impact of border measures to prevent the importation of pathogens is needed to support the evaluation of policy options.
Containment	Research on the effectiveness of population level testing (e.g. for Covid-19 and other respiratory pathogens) is needed to support the testing of containment-based policy options for pandemic response.
Containment and mitigation	Research to assess the relative effectiveness of individual control measures introduced in response to the Covid-19 pandemic, and their potential efficacy for other pathogens, will be needed both to inform future policies/plans and to support the updating of pandemic models. Currently, given the introduction of packages of measures during the pandemic response, information on the effectiveness of individual measures is limited.
Waterborne pathogens	Research to identify which novel pathogens, either imported or potentially endemic in the future due to changing climatic conditions, might pose a risk due to resistance to current treatment technologies used in the UK water supply.
Increased mortality due to insufficient healthcare	Mortality rates are likely to increase substantially should healthcare capacity be exceeded in an extreme unmitigated pandemic RWCS. Research is needed to understand this relationship and incorporate it into planning scenarios.

Medicines and vaccines for pandemics and HCID outbreaks not licensed in the UK that should be reviewed in 12 months

39. In reviewing available medicines and vaccines, the Medicines Subgroup recommended that these products be subject to periodic review regarding future stockpiling options, the first of those reviews occurring in 12 months:

    f. Pocapavir, an experimental agent available in the US and through the WHO for emergency compassionate use in immunocompromised patients with chronic enteroviral infection.

    g. Ervebo, an Ebola (Zaire strain) vaccine that the UK can currently access (If necessary) through the WHO but which is not currently available for domestic stockpiling.

    h. Zabdeno/Mvabea, a two-compound immunisation schedule for Ebola (Zaire strain) that is licenced in the EU.

    i. Mvabea, a possible vaccine for Marburg virus that might be considered alongside Ebola virus vaccine options.

Medicines and vaccines in development that are of interest for horizon scanning

40. While gathering expert advice for this review of medical countermeasures, a number of medicines in development were identified. The Medicines Subgroup recommends that progress on these products is monitored as they may present options for future improvements in the coverage and resilience of any stockpiles.

PPE

41. Fit testing at the scale necessary is a huge task and requires more detailed work to develop a feasible implementation model. It is recommended that further work is commissioned to develop advice on:

    j. Incorporation of widespread fit testing within BAU NHS and ASC provision within existing resource or with a minor uplift in resource;

    k. Target percentage baseline levels of fit testing across groups (such as ICU, A&E, etc.) to be achieved and maintained;

    l. Contingency plans for emergency surge fit testing capabilities to supplement higher baseline levels in a pandemic;

    m. Other complementary IPC practices that should be considered alongside enhanced PPE; and

    n. A research programme to support the evidence base on effective PPE use and associated IPC practice.