The "Consensus on Emergency-Mode Pharmacy Intravenous Admixture Service (PIVAS) in the Context of Public Health Emergencies" (hereinafter referred to as the "Consensus") was developed by the Department of Pharmacy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, and Centralized PIVAS Expert Group of National Pharmaceutical Affairs Management Professional Quality Control Center, discussed and revised repeatedly by pharmacy experts in several meetings. The "Consensus" aimed at clarifying the significance of centralized PIVAS for medical institutions at all levels when responding to public health emergencies and providing reference on optimizing and reforming work processes, ensuring the safety of intravenous agents, improving the quality of pharmaceutical services, and ensuring the health of medical staff for medical institutions at all levels under different infrastructure conditions.

Consensus on Emergency-Mode Pharmacy Intravenous Admixture Service (PIVAS) in the Context of Public Health Emergencies

Centralized PIVAS Expert Group of National Pharmaceutical Affairs Management Professional Quality Control Center

The COVID-19 pandemic is a major public health emergency with the fastest spread, the widest range of infection and the most difficulties in prevention and control in China since 1949. The intravenous drip administration, delivering medicines directly to the circulatory system, possesses advantages of rapid onset, controllable doses and speed. It can quickly replenish body water, electrolytes, energy, and nutrients, and adjust acid-base balance. It is often used in drug therapies where rapid response is required, and patients cannot be administered orally or by injection. It also plays an important role in treating critically ill patients during public health events including outbreaks of acute infectious diseases.

Traditionally, intravenous admixture is completed by the nursing staff in a non-clean and open dispensing room of the ward. Despite of defects and shortcomings, this still meets routine needs for intravenous therapies. However, during an outbreak of acute infectious diseases, some viruses could be spread through air droplets. This traditional process done in wards may increase the risk of liquid medicine contamination, causing cross-infection in the hospital. Besides, the increase in the number of clinical admixture personnel and the upgrade of their protective measures may make liquid preparation more difficult. In addition, the number of patients would inevitably soar during such outbreaks, many of whom severely ill. Thus, nurses would be required to directly participate in healthcare services, which renders the traditional way inappropriate to meet the needs of clinical work.

On the other hand, the centralized pharmacy intravenous admixture service (PIVAS) mode, not affected by the ward conditions, could ensure a clean environment during the admixture, thereby reducing the risk of nosocomial cross-infection, improving the efficiency of personnel deployment, and enabling nursing staff's direct participation in healthcare services. It would, at the same time, protect nursing staff from occupational exposure and environmental pollution in ward zones. Centralized PIVAS undertaken by pharmacy professionals will improve the quality of clinical medication orders, ensure the quality of infusion products, promote rational use of medication, and guarantee patient medication safety.

1 Significance of establishing a centralized PIVAS site in the context of public health emergencies
1.1 Definition of public health emergencies. It refers to major infectious disease outbreaks, mass diseases of unknown causes, major food and occupational poisonings, and other events which seriously affect public health that occur suddenly and cause or may cause serious damage to public health [1].
1.2 Advantages of centralized PIVAS. In public health emergencies, nurses are under dual pressure of increased workload and infection risk. To ensure the safety of agent admixture under such pressure and the quality of infusion products, a centralized PIVAS site should be established. Advantages are as follows: ① The clean zone and non-clean
control zone of the "centralized PIVAS site" have strict requirements on the floor, object surface, air suspension, the number of pathogens, and various technical operations, which is not only significant in reducing the impact of environmental pollution on the safety of intravenous medication [2-4], but also in improving the occupational protection of medical staff; ② Without wearing heavy protective equipment, nurses could perform admixture without being affected by restrictions of movement; ③ Centralized management of all links improves efficiency and reduces errors [3-4]; ④ Centralized deployment and special-person delivery could optimize human resource allocation.

2 Emergency workflow for centralized PIVAS in medical institutions under different infrastructure conditions

2.1 A medical institution that has already established a PIVAS center and whose scale meets its intravenous medication needs should strictly implement the No. 62 document issued by the National Health Commission "Quality Management Standards for Centralized PIVAS" (referred to as "Standards") and the attached "Operating Procedures for Centralized PIVAS" (referred to as "Operating Procedures"), as well as the "Guidelines for the Building and Management of PIVAS Centers" formulated by the National Hospital Pharmacy Management Professional Quality Control Center Group (Refer to as "Guidelines").

2.2 A medical institution that has already established a PIVAS center, but whose scale fails to meet its intravenous medication needs should reform its existing processes.

2.2.1 Significance of process reform. In the context of infectious disease outbreaks and public health events, types and quantities of clinical intravenous agents change dramatically. When the service capacity and equipment configuration of PIVAS' original design fails to meet the needs of independent preparation of various drugs in different regions, emergency adjustments should be made to the existing PIVAS processes based on actual conditions to meet clinical needs. Thanks to the fact that the environment of a PIVAS site is cleaner than that of the ward's dispensing room, the centralized mode after emergency adjustment may better ensure the safety of clinical intravenous medication.

2.2.2 Hardware system adjustment. During infectious disease outbreaks, the clean zone in a PIVAS center should have an independent fresh air supply system operating normally; the use of the control zone should be determined according to the operation mode of its central air-conditioning system. The whole air system should operate normally if the filters are running at or above medium efficiency or keep the air return turned off while the fresh air at the maximum efficiency [5].

In accordance with the requirements of relevant regulations, a PIVAS center should be equipped with a special liquid admixture console for dosing and compounding. That is, it should be equipped with a hundred-level laminar flow table for the preparation of ordinary infusion and parenteral nutrition, and a class II A2 type hundred-level biological safety cabinet to prepare hazardous agents and antibiotic infusions. During infectious disease outbreaks, when the number of dispensing consoles in the original PIVAS configuration fails to meet the needs of intravenous admixture, a dispensing console or table in the PIVAS clean zone can be temporarily added. If it is not possible to add one due to space, air supply restrictions and other reasons, drug types can be temporarily adjusted corresponding to the console. That is, antibiotics can be prepared in a horizontal laminar flow table with the fan being turned off, while common agents in a biological safety cabinet. However, hazardous drugs must be prepared in a biological safety cabinet, while parenteral nutrition (non-industrial prepared) in a horizontal laminar flow console. Allergic agents such as penicillin must be prepared separately and cannot be mixed with others. After the preparation of hazardous drugs is completed, all discarded needles must be placed in a box for sharps in the operating area of the biological safety cabinet. Penicillin bottles, ampoules, syringes, and gloves are to be individually packaged in yellow bags for medical waste and treated uniformly according to regulations.

2.2.3 Workflow is shown in figure 1.

2.3 A medical institution that has not established a PIVAS center or cannot provide PIVAS due to limited conditions should set up a temporary site for centralized PIVAS.

2.3.1 Significance of setting up a temporary site for centralized PIVAS. In the context of infectious disease outbreaks, considering the potential safety hazards of liquid medicine pollution due to poor air quality in the dispensing rooms of scattered wards, and the heavy workload of nursing staff, a clean and temporary site should be chosen according to the actual situation for centralized PIVAS to ensure the safety of intravenous medication for patients.

2.3.2 Methods to set up a temporary site for centralized PIVAS.

① Site selection. It is preferred to locate the temporary site in a region where there is a clean air-conditioning system that can operate normally (with a cleanliness level of 100,000 and above) and is convenient for drug delivery. If the above requirements cannot be met, choose an independent area close to the inpatient pharmacy, far from the quarantine wards, with clean and pollution-free surroundings and is convenient for drug delivery. The site area should be adapted to the daily quantity of PIVAS under emergency conditions, with access to network and sound water and electricity supplies. For specifics, please refer to the "Guidelines". ② Facilities and equipment. The site should be equipped with computers, printers, telephones, preparation consoles, medicine carts, sorting racks, baskets, and lockers. ③ Functional partition. The temporary site should be divided into clean zone, non-clean control zone and supportive work zone. For specifics, please refer to the "Guidelines".

2.3.3 Workflow of a temporary centralized PIVAS site is shown in figure 2.

2.3.4 Notes for the mode of centralized PIVAS. ① Pharmacy adjustment. In the context of public health emergencies, especially during an outbreak of acute infectious diseases, the number of operating pharmacies should be reduced to a minimum level. The quantity of basic IV products should be supplemented according to the base number and placed in a special drug transfer warehouse set up in the temporary site for convenience consideration. ② Sorting adjustment. To enhance work efficiency, pharmacists in the inpatient pharmacy should
preliminarily divide agents into intravenous drip and non-intravenous drip according to "routes of administration". Non-intravenous drip should be transferred to the ward by specially assigned personnel, while intravenous drip should be sent to the temporary centralized PIVAS site by specially assigned personnel for follow-up operations, including unpacking, labeling, sorting, verification, mixing and dispensing, and product packaging.

3 Environmental sanitation management in the emergency mode of centralized PIVAS. During infectious disease outbreaks, the spread of the disease can be prevented effectively by reducing or cutting off routes of transmission and strengthening cleanliness and disinfection control.

3.1 Classification of disinfectants. Disinfectants are agents that kill microorganisms on the media to achieve requirements for disinfection or sterilization. According to their active ingredients, they can be divided into alcohol disinfectants, chlorine disinfectants, iodine disinfectants, peroxide disinfectants, guanidine disinfectants, phenol disinfectants, quaternary ammonium salt disinfectants, and others. According to their purposes, they can be divided into surface disinfectants, medical device disinfectants, air disinfectants, hand disinfectants, skin disinfectants, mucous membrane disinfectants, foci disinfectants, and others.

3.2 The choice of commonly used disinfectants. Disinfectants of the same class possess different mechanisms and effects on pathogenic microorganisms. Table 1 shows the types of disinfection supplies corresponding to common disinfection objects in centralized PIVAS sites. In addition, appropriate classes of disinfectants and concentrations should be selected according to types of disinfection objects and requirements, as is shown in Table 2.

3.3 Disinfection of the centralized PIVAS site. According to the requirements for the prevention and control of infectious diseases and the severity of the epidemic, centralized PIVAS sites in medical institutions under different infrastructure conditions should establish disinfection principles for various regions and levels. In addition to "Standards" and "Technical Standards for Disinfection in Medical Institutions" and other relevant requirements, the frequency and intensity of disinfection should be increased, the air and surface of objects should be cleaned and disinfected, disinfection services for personnel should be provided to maintain cleanliness of the environment and avoid the risk of nosocomial cross-infection.

3.3.1 Clean zone. A clean zone involves a preparation room, preliminary dressing room, second time dressing room, laundry and sanitary ware room. Air disinfection purifiers should be equipped according to routes of transmission, and effective disinfectants according to types of pathogenic microorganisms. Increase the times of disinfection for floors, walls, ceilings, doors and windows, and consoles; increase the times of sedimentation bacteria monitoring and the number of pathogen indicators; and increase the frequency of disinfection and replacement of basic- and medium-efficiency filters.

<table>
<thead>
<tr>
<th>Objects for disinfection</th>
<th>Type of disinfection supplies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface of objects</td>
<td>Alcohol, chlorine, peroxide, and quaternary ammonium salt disinfectant</td>
</tr>
<tr>
<td>Indoor air</td>
<td>Peroxide disinfectant</td>
</tr>
<tr>
<td>Hand, skin</td>
<td>Alcohol, iodine-containing, and quaternary ammonium salt disinfectant</td>
</tr>
<tr>
<td>Mucosa, wound</td>
<td>Iodine, alcohol, and peroxide disinfectant</td>
</tr>
<tr>
<td>Work clothes</td>
<td>Chlorine disinfectant</td>
</tr>
<tr>
<td>Paper, prescription</td>
<td>Ethylene oxide</td>
</tr>
</tbody>
</table>

3.3.2 Non-clean control zone. A non-clean control zone involves areas for order review, infusion label printing, drug placement verification, infusion product verification, packaging and delivery.

3.3.3 Supportive work zone. ① Buffer zone. This includes channels for infusion product transportation, entries, exits, and unpacking area. Increase the intensity and frequency of air disinfection according to routes of transmission; select effective disinfectants according to types of pathogens, and increase the disinfection times for floors, walls, transfer carts, and before unpacking. ② Living zone. Increase the intensity and frequency of air disinfection according to routes of transmission; select effective disinfectants according to types of pathogens, and increase the disinfection times for floors, walls and desktops; strengthen anti-rat, fly, and mosquito facilities and management; reduce population density and avoid group dining.

3.4 Waste disposal. According to the "Medical Waste Management Regulations", wastes should be classified based on their nature and collected in special plastic bags before being treated uniformly by medical institutions. During an epidemic, pay attention to the cleaning and disinfection of waste collection barrels in various regions, and appropriately increase the times of disinfection.

3.5 Others. For medical institutions without PIVAS centers, a temporary centralized site should be established and disinfected according to requirements for non-clean control zones, and other areas according to those for buffer zones and living zones.

4 Personnel protection management. Carry out training and assessment of knowledge related to the prevention and control of infectious diseases and monitor the health status of medical staff.

4.1 Carry out training and assessment of knowledge. Carry out trainings on laws and regulations related to public health emergencies for personnel in the centralized PIVAS site; on epidemiology, routes of transmission, initial symptoms, disinfection, isolation, quarantine, and protection skills; and on centralized PIVAS process in accordance with the Standards and Guidelines. Carry out regular assessment on infection prevention and control. Those who fail should be re-trained until the assessment is passed.
4.2 Personnel monitoring and protective measures. Establish personal health records and monitoring mechanisms; equip on-the-job medical staff with thermoflashes to dynamically monitor their health status daily, including fever, cough, diarrhea and other initial symptoms of acute infectious diseases. Abnormality of any indicator should be reported in time for further medical examination and evaluation. All passages should be equipped with quick-drying hand disinfectants, and hand hygiene and disinfection should be strictly implemented. The personnel involved in the centralized PIVAS site should take appropriate protections according to the characteristics of the working environment. Medical staff in non-clean control zones should wear special work clothes, disposable medical caps, medical surgical masks, and disposable isolation gowns and gloves if possible [9]. Dust-proof clothes can also be used when isolation gowns are in short supply. Staff in the clean zone should strictly implement relevant requirements in the "Operating Regulations".

4.3 Psychological counseling. Pay attention to the physical and mental health of medical staff, carry out mental health assessment, strengthen psychological assistance, and perform targeted intervention and psychological counseling to reduce psychological pressure.

4.4 Shift optimization. Implement a group shift system, with relatively fixed daily on-call and standby personnel, without interfering with each other. Set up a mobile emergency response team to deploy manpower timely according to daily workload and actual conditions.

5 Notes for the emergency mode of centralized PIVAS

5.1 Work mode adjustment. The working hours for the centralized PIVAS site should cover the needs of intravenous medication in the wards 24/7. Besides dealing with regular long-term medical orders in batches, preparations of agents on temporary orders should be added. For agents on emergent temporary orders or poorly stable ones, an immediate delivery method should be adopted to make quick delivery to the ward in need. Non-emergency temporary medical orders should be deployed in batches. The number of deployments should be increased as many as possible, and the interval between batches should be reduced to ensure the quality of infusion products.

5.2 Emergency adjustment of the software system. If the existing PIVAS software system meets the emergency needs, the original work process should be adopted and completed in strict accordance with the "Operational Procedures." If the software system fails to meet the emergency needs, the pharmacy workstation of the hospital information system (HIS) and the nurse workstation can be temporarily integrated to manually process temporary and long-term medical orders in batches, and strengthen the verification for the deployment, sorting, entry of storage, exit of storage, and packing.

5.3 Order review. Pharmacists need to review the legality, standardization, and suitability of medical orders. Specific processes are shown in Figure 3. When facing some special problems, including medical team from other hospitals perform offsite practices and medical cross-infection of paper orders, the pharmacy department should focus on the suitability of the medical order based on the establishment of interim management regulations, the approval of the pharmacy management team, and the filing with the medical administrative department.
Clinical pharmacists should actively participate in the formulation of clinical drug treatment plans. For off-label use, pharmacists should assist physicians in in-depth analysis of the pros and cons of the treatment plan, and fully consider possible adverse reactions of such use. For this reason, pharmacists should pay attention to the following when reviewing medical orders: ① Strictly review the incompatibility and interactions between the main therapeutic traditional Chinese and Western medicines recommended in the diagnosis and treatment guidelines and other commonly used medicines. Review and sort out authoritative scientific evidence, including the best evidence-based practices currently available; scientific argument in Pharmacoeconomics; authoritative multi-center research results or diagnosis and treatment guidelines and sufficient authoritative literature reports; long-term clinical practice scientific evidence and others, to compile relevant documents for physicians’ reference; ② Establish an emergency record-keeping mechanism for off-label use with a simple process to review the dosage, frequency, route of administration, dissolution volume, drug concentration for patients with infectious diseases, especially critically ill. When the mechanism is filed, it should be quickly reviewed and approved. ③ For therapeutic drugs whose advantages outweigh disadvantages, the review of some contraindications can be exempted. ④ For drugs that have been approved for clinical trials, the review content of off-label use can be quickly passed after filing.

5.4 Drug supply. The pharmacy department should formulate a list of key therapeutic drugs under public health emergencies based on the national diagnosis and treatment guidelines and clinical needs, to achieve targeted drug preparation and deployment [10]. The following principles should be followed for the centralized PIVAS: ① Preferably select pre-mixed agents and industrialized multi-chamber infusion products to reduce the needs for puncture dosing. ② When purchasing and restoring basic infusions, the third and fourth generations of fully enclosed products should be selected, including soft bag and stand-up bag products, to avoid contact between the liquid and environmental air during infusion. ③ Minimize the use of similar medicines, avoid medicines with similar appearance and names, avoid errors due to multi-specification of one medicine.

5.5 Strengthen visual management. To rapidly adapt to temporary process reforms and ensure standardized operations under emergencies, visual management should be strengthened. Post centralized PIVAS-related regulations, standard operating procedures of equipment and software, and precautions in prime locations. Visual management should also be strengthened for interim regulations, precautions, and standard operating procedures regarding regional divisions, placement of equipment and facilities, placement of medicines, and hospital infection control after process reform. All these should be removed in time after the emergency is lifted.

5.6 The entry and exit of personnel and items. In the centralized PIVAS site, this shall be strictly complied with relevant regulations and requirements of the "Standards" and "Guidelines". Staff should perform strict hand disinfection before entering and exiting the supportive work zone, the non-clean control zone and the clean zone. Surface of medicine products and tools should be disinfected before entering the non-clean control zone from the buffer zone and the clean zone from the non-clean control zone. The surface of medicine boxes delivered to the PIVAS site should be strictly disinfected before unpacking. To reduce cross-contamination in the circulation of medicines, personnel, and tools from the ward to the centralized PIVAS site, infusion products should be packaged with disposable plastic bags (or cartons) before delivery, so that drugs and containers can be distributed from the site to the ward in a one-way manner. In addition, a segmented delivery method should be adopted according to regional divisions, and the flow of personnel should not be crossed. If possible, medical institutions can use non-contact methods, including drug delivery robots, rail logistics or pneumatic tube logistics for drug delivery, and disinfection management should be strengthened.

6 IT development helps respond to public health emergencies. Medical institutions should use information technology as much as possible to make the centralized PIVAS more convenient, efficient and accurate.

6.1 Establish a temporary authorization mechanism for orders to implement electronic signatures and paperless orders. Establish a paperless order process for medicines to reduce contact with potential infectious agents in the ward during pharmaceutical services and minimize the risk of infection exposure. Use certificate authority (CA) services to collect electronic signatures of physicians and pharmacists; establish a temporary authorization mechanism for orders for medical team members from other hospitals, and temporarily authorize them to log in to the physician’s workstation with a personal password; electronic signature could be signed immediately after physician's confirmation of the order and pharmacist's reviews [11-13].

6.2 Barcode technology-assisted drug withdrawal. Medical institutions with appropriate conditions can use barcode scanning technology to finely manage drug withdrawal [14]. Drugs that have been mixed and prepared or those that have been sent to the quarantine ward are not accepted for withdrawal applications.

6.3 IT-supported process control. Relying on the hospital information system structure and the information management system of the PIVAS center, medical institutions should use barcode technology as much as possible to realize the whole process information management from order review, infusion preparation, exit of storage review, ward reception, to patient administration, to meet clinical needs under emergency quickly and efficiently [8].

6.4 Remote maintenance and emergency response. To deal with information system problems encountered in the centralized PIVAS site during public health emergencies, and to prevent the inconvenience caused by cross-infection and traffic obstacles, the information system should be equipped with remote maintenance and emergency response functions [15].

7 Conclusions
Centralized PIVAS not only ensures the quality of infusion products, promotes rational use of medications, optimizes the allocation of human resources, and improves the quality of pharmaceutical services, but also strengthens the professional protection of medical personnel. This is an inevitable trend in the development of intravenous admixture. During public health emergencies, the emergency-mode of centralized PIVAS exerts unique advantages and functions. To enhance capabilities to respond to such emergencies, medical institutions should build a centralized PIVAS site following the "Standards" and "Guidelines" and considering the actual needs for intravenous agents to ensure the safety of intravenous agents.
The writing group of “Expert Consensus on Emergency-Mode Centralized Pharmacy Intravenous Admixture Service (PIVAS) in the Context of Public Health Emergencies”: Writing team leaders: Liu Dong, Yan Qing, Wu Yongpei List of expert members: (Sorted by phonetic alphabet of last name) Bao Jiatan, The First Affiliated Hospital of Suzhou University Du Guang, Tongji Xianhong Hospital, Huazhong University of Science and Technology Dong Mei, Affiliated Tumor Hospital of Harbin Medical University Dong Zhanjun, Hebei Provincial People’s Hospital Fang Hongmei, Run Run Shaw Hospital, Zhejiang University School of Medicine Feng Wei, The First Affiliated Hospital of Xi’an Jiaotong University Gong Xuepeng, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology Hu Luohong, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology Li Guochun, Affiliated Hospital of Traditional Chinese Medicine, Southwest Medical University Li Juan, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology Liu Dong, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology Liu Guangxuan, Liaoning Provincial Cancer Hospital Liu Wei, Beijing Shijitan Hospital, Capital Medical University Liu Xinchun, Qilu Hospital of Shandong University Sun Lulu, Pharmaceutical Affairs Management Research Department, Hospital Management Research Institute, National Health Commission Wang Gang, Children’s Hospital of Chongqing Medical University Wu Yongpei, Pharmaceutical Affairs Management Research Department, Hospital Management Research Institute, National Health Commission Xia Hong, The First Affiliated Hospital of University of Science and Technology of China Yan Qing, Pharmaceutical Affairs Management Research Department, Hospital Management Research Institute, National Health Commission Yang Wei, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou Zhang Jianzhong, Zhongshan Hospital Affiliated to Fudan University Zhang Jian, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine Zhang Jun, The First Affiliated Hospital of Kunming Medical University Zhang Ruihua, Pharmaceutical Affairs Management Research Department, Hospital Management Research Institute, National Health Commission Zhang Wenjun, General Hospital of Tianjin Medical University

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