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## ORGANIZATION OF THE QUALITY ASSURANCE SYSTEM OF COMPOUNDING PHARMACIES IN UKRAINE: RESULTS OF THE SURVEY

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*Key words: compounding preparations; quality assurance system; survey*

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*To meet the needs of patients for treatment of a number of diseases compounding preparations are often used. The aim of our study was to determine the possibility of introduction of the international experience of forming the quality assurance system for compounding preparations in conditions of compounding pharmacies of Ukraine. For this purpose the survey of employees of compounding pharmacies regarding organization of the quality assurance system for compounding preparations has been conducted. In the survey 93 employees of compounding pharmacies took part. The research was conducted in 12 regions of Ukraine in 2013-2014. The questionnaire contained 44 questions, which represented the statements of organization of the quality assurance system of compounding pharmacies of Ukraine and compounding preparations. The statements were divided into 10 groups: personnel and training, premises and equipment, documentation, production, complaints and product recalls, self audits, in-pharmacy quality control, work contracted out, the necessary requirements of the State Pharmacopoeia, overarching statements. For the collection and processing of data 4-point Likert scale was used. The statement was considered to be accepted if more than 50% of respondents chose "A – strongly agree" or "B – agree". The survey of employees of compounding pharmacies concerning the possibility of introducing the international experience of the quality assurance system for compounding preparations has allowed to determine and estimate their attitude to the statements proposed, to identify the points of discussion. Processing of the results of the survey has shown that all 44 statements were approved by more than 71.0% of the respondents. Each statement received an average of 94.9% of "A" or "B". And 22 statements (50.0%) had 100.0% agreement "A" + "B".*

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To meet the needs of patients for treatment of a number of diseases the magistral formulas are often used together with manufactured medicines. Worldwide compounding preparations are applied in various fields of medicine: hormone replacement therapy, dentistry, dermatology, oncology, pediatrics, geriatrics, physiotherapy, medical cosmetology, sports medicine, allergies treatment, and others; as well as in veterinary medicine [15, 17, 19, 21, 22, 24].

It is known that quality assurance is the combination of organizational arrangements taken to ensure quality conformance of drugs with their purpose [11, 23]. The quality assurance system of compounding preparations is the system of steps and corresponding actions, which guarantee the necessary quality for drug preparation. Nowadays creation of programmes and implementation of quality assurance systems for compounding preparations are urgent in the USA, EU, Japan, UK, etc. [9, 14, 16, 23].

The quality assurance system for compounding preparations must ensure development and technology of compounding preparations in accordance with the latest achievements of science; preparation and control operations are clearly specified and implemented according to the principles of Good Preparation Practice; dispensing only those compounding preparations, which are correctly prepared, checked and stored in accordance with the procedures approved and prepared by a competent person; the use of appropriate equipment, containers, ac-

tive substances and excipients, packaging material, it allows preparation, storage, use of compounding preparations in such a way as to provide the required quality throughout the shelf-life and in-use expiry dates; good documentation practice [23].

Taking into consideration the experience of Ukraine regarding the implementation of appropriate Good Practices (G<sub>x</sub>P) [12] for manufactured drugs it is obvious that some difficulties can appear when introducing the quality assurance system for compounding preparations; therefore, when organizing standards it is necessary to consider the legislation and experience of compounding pharmacies of the USSR, and harmonization with the international standards.

The aim of our study was to determine the possibility of introduction of the international experience of forming the quality assurance system for compounding preparations in conditions of compounding pharmacies of Ukraine.

### Materials and Methods

For this purpose the survey of employees of compounding pharmacies regarding organization of the quality assurance system for compounding preparations was conducted. The questionnaire was developed taking into account the main statements of the PIC/S documents related to preparation of drugs in conditions of pharmacies, modern legislative base of compounding

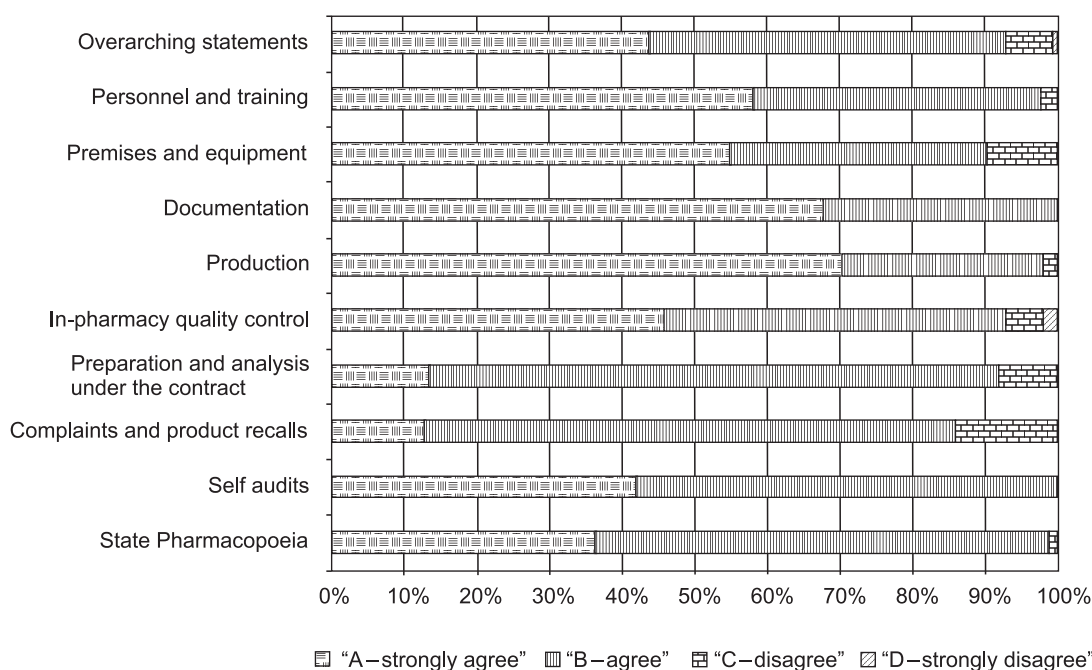


Fig. Distribution of the respondents' answers concerning the statements proposed for the quality assurance system of compounding preparations.

preparations in Ukraine, the experience of US and British Pharmacopoeias [11, 13, 20]. The experience of survey hospital pharmacists from 85 countries of the world was also used, its results were presented at the International Congress of FIP "Global Conference Future of Hospital Pharmacy" (Switzerland, Basel, 2008). The Ukrainian pharmacists did not participate in this questioning [18].

The questionnaire method was used in our study, 93 employees who worked or had experience of work in compounding pharmacies responded to the survey. The average work experience of the respondents in the compounding pharmacy was 18 years. The research was conducted in 12 regions of Ukraine (Volyn, Dnipropetrovsk, Donetsk, Zakarpattia, Kyiv, Luhansk, Rivne, Sumy, Ternopil, Kharkiv, Cherkasy, Chernihiv) in 2013-2014.

There were 44 questions in the questionnaire, which represented the statements of organization of the quality assurance system of compounding pharmacies of Ukraine and compounding preparations. The statements were divided into 10 groups: personnel and training (7 questions), premises and equipment (1 question), documentation (2 questions), production (5 questions), complaints and product recalls (3 questions), self audits (2 questions), in-pharmacy quality control (5 questions), preparation and analysis under the contract (2 questions), the necessary requirements of the State Pharmacopoeia (8 questions) and overarching statements containing questions (9 questions), which were not included in other groups.

For the collection and processing of data 4-point Likert scale was used: "A – strongly agree with statement"; "B – agree"; "C – disagree"; "D – strongly disagree with statement". The statement was considered to be accepted if more than 50% of respondents chose "A – strongly agree" or "B – agree".

## Results and Discussion

Processing of the results of the survey has shown that all 44 statements were approved by more than 71.0% of the respondents: "A – strongly agree" or "B – agree" (Fig.). Each statement received an average of 94.9% of "A" or "B". Only 174 (4.3%) of 4092 answers were "C – disagree" and 15 (0.4%) "D – totally disagree"; at the same time there were 1870 positive answers (45.7%) "A – strongly agree", and 2033 (49.6%) "B – agree". And 22 statements (50.0%) had 100.0% agreement "A" + "B". The minimum level of consensus A + B in all statements was 71.0%.

According to the results of the survey the revival of practical preparation of compounding preparations and use new active ingredients when preparing compounding and creation of programme of extension use of compounding preparations for oncology, pediatrics, geriatrics, veterinary are urgent (93.6%). At present there is a necessity to update formulations of compounding preparations and use new active ingredients when preparing compounding preparations (87.1%), although during the survey 12 respondents noticed that this task should be solved with participation of scientists and physicians, as well as research for improving methods and systems of preparation and quality assurance of compounding preparations.

*Personnel and training.* According to the survey 100.0% of the respondents approved education and advanced training of pharmacists based on last scientific research; the curriculum should include the course of quality assurance of compounding preparations. The cases of the staff incompetence in compounding pharmacies should be investigated, solved through strategic research and made public for the purpose of prevention of reappearance (93.6%). 90.3% of the respondents

agreed with the statement concerning participation of pharmacists in improvement of methods of preparation and quality control of compounding preparations, it reflected the experience of the quality assurance system introduced in compounding pharmacies of the USA.

During the research challenges of implementation of requirements for *premises and equipment* and *preparation process* in compounding pharmacies were identified. The preparation process should be based on the requirements of GMP. Based on the results obtained it has been found that these statements require significant investment and should be harmonized with the existing ones in Ukraine [2, 3].

According to the results of the survey 100.0% of the respondents supported the need for good *documentation* practice and development and implementation of documented standard operating procedures (SOP) for all activities in the compounding pharmacy in preparation, quality control, labeling, storage, purification, disinfection, qualification, and work with the equipment, etc.

Appreciation of the majority of pharmacists concerning creation of the reporting system about rejected low-quality compounding preparations (80.7%), *product recalls* and *self audits* in order to improve the quality and safety of drug treatment practice and prevent re-occurrence of such error (100.0%), the risk assessment of preparation and quality control of compounding preparations is important [6].

Since one of the ways of quality assurance of extemporaneous medicines is development and introduction of general articles and monographs on officinal formulas to the National Pharmacopoeia [8], the questions related to development and improvement of general articles on sterile and nonsterile compounding preparations, dose regimen [4, 5], introduction of monographs on officinal formulas of compounding preparations taking into account the needs of modern compounding pharmacies were included into the questionnaire. 96.8% of the respondents were agreed with the statement about urgency of forming the conception of determination of shelf life and stability for sterile and nonsterile compounding preparations [7]; 100% of the respondents were agreed with the statement about the order of conducting experimental research.

According to the results of the questionnaire, the statements about *preparation and analysis under the contract* were not fully supported by the respondents since to conduct analysis in a certified laboratory for drug quality control will lead to significant increase of costs.

*In-pharmacy quality control.* According to the respondents all prescriptions and orders of medical preventive institutions must be double checked before preparation and dispensing (100.0%).

A physician and a clinical pharmacist should take into account the compatibility of the compounding preparations prescribed with the manufactured drug, and, if necessary, with herbal drugs and diets (71.0%).

The statements about development and validation of analytical methods taking into account the capabilities of the material and technical base of compounding pharmacies (96.8%), substantiation of the possibility of using non-pharmacopeial methods, qualification of analytical equipment (photocolorimetry, refractometry and polarimetry for assay) are very urgent [1, 10]. Development of such methods will contribute to save funds of compounding pharmacies. In case of external inspections of pharmacies or conducting the stability studies of compounding preparations other specific developed and validated methods, which can be reproduced in laboratories for drug quality control, should be used (100.0%).

#### CONCLUSIONS

1. The survey of employees of compounding pharmacies concerning the possibility of introducing of the international experience of the quality assurance system of compounding preparations has allowed to determine and estimate their attitude to the statements proposed, to identify the points of discussion.

2. Processing of the results of the survey has shown that all 44 statements proposed concerning the quality assurance system of compounding preparations were approved by more than 71.0% of the respondents: "A – strongly agree" or "B – agree". Each statement received an average of 94.9% of "A" or "B". And 22 statements (50.0%) had 100.0% agreement "A" + "B".

3. According to the results of the survey it has been found that the question of material costs is an important factor for implementation of the quality assurance system of compounding preparations.

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#### **ОРГАНІЗАЦІЯ СИСТЕМИ ЗАБЕЗПЕЧЕННЯ ЯКОСТІ ВИРОБНИЧИХ АПТЕК В УКРАЇНІ: РЕЗУЛЬТАТИ АНКЕТУВАННЯ**

**О.А.Здорик**

**Ключові слова:** екстемпоральні лікарські засоби; система забезпечення якості; анкетування

Для задоволення потреб пацієнтів при низці захворювань використовуються екстемпоральні лікарські засоби (ЕЛЗ). Метою дослідження було визначення можливості впровадження міжнародного досвіду формування системи забезпечення якості ЕЛЗ в умовах виробничих аптек України. Для досягнення мети було проведено анкетування співробітників виробничих аптек України щодо організації системи забезпечення якості ЕЛЗ. В опитуванні взяли участь 93 співробітники виробничих аптек. Дослідження проводили в 12 областях України у 2013-14 рр. Анкета включала 44 питання, які висвітлювали положення організації системи забезпечення якості виробничих аптек України та ЕЛЗ. Наведені положення були розподілені на 10 груп: персонал та навчання, приміщення та обладнання, документація, виготовлення, скарги та відкликання продукції, самоінспекція, внутрішньоаптечний контроль якості, виготовлення та аналіз за контрактом, необхідні вимоги Державної фармакопеї, загальні положення. Для збору та обробки голосів використовували 4-и бальну шкалу Лайкерта. Положення вважали прийнятими, якщо більше 50% голосів відповідали варіантам «А – абсолютно згоден» і «В – згоден». Анкетування співробітників виробничих аптек щодо визначення можливості впровадження міжнародного досвіду системи забезпечення якості ЕЛЗ дозволило встановити і оцінити їх ставлення до запропонованих положень, виявити дискусійні питання. Обробка результатів опитування показала, що всі 44 запропонованих положення отримали більше 71,0% схвальних голосів респондентів. Кожне положення отримало у середньому 94,9% голосів «А» або «В». 22 положення (50,0%) отримали 100,0% схвалення «А» + «В».

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#### **ОРГАНИЗАЦИЯ СИСТЕМЫ ОБЕСПЕЧЕНИЯ КАЧЕСТВА ПРОИЗВОДСТВЕННЫХ АПТЕК В УКРАИНЕ: РЕЗУЛЬТАТЫ АНКЕТИРОВАНИЯ**

**А.А.Здорик**

**Ключевые слова:** экстемпоральные лекарственные средства; система обеспечения качества; анкетирование

Для удовлетворения потребностей пациентов при ряде заболеваний используются экстемпоральные лекарственные средства (ЭЛС). Целью исследования было определение возможности внедрения международного опыта формирования системы обеспечения качества ЭЛС в условиях производственных аптек Украины. Для достижения цели было проведено анкетирование сотрудников производственных аптек касательно организации системы обеспечения качества ЭЛС. В опросе приняли участие 93 сотрудника производственных аптек. Исследование проводили в 12 областях Украины в 2013-14 гг. Анкета содержала 44 вопроса, которые отображали положения по организации системы обеспечения качества

*производственных аптек Украины и ЭЛС. Приведенные положения были распределены на 10 групп: персонал и обучение, помещение и оборудование, документация, изготовление, жалобы и отзыв продукции, самоинспекция, внутриаптечный контроль качества, изготовление и анализ по контракту, необходимые требования Государственной фармакопеи, общие положения. Для сбора и обработки голосов использовали 4-х балльную шкалу Лайкерта. Положения считали принятыми, если более 50% голосов отвечали вариантам «А – абсолютно согласен» и «В – согласен». Анкетирование сотрудников производственных аптек по определению возможности внедрения международного опыта системы обеспечения качества ЭЛС позволило установить и оценить их отношение к предложенным положениям, выявить дискуссионные вопросы. Обработка результатов опроса показала, что все 44 предложенные положения получили более 71,0% согласия респондентов. Каждое положение получило в среднем 94,9% голосов «А» или «В». 22 положения (50,0%) получили 100,0% согласия «А» + «В».*