

GLOBAL AND NATIONAL BONE MARROW REGISTRIES: EXPERIENCE OF USING, MAIN ISSUES, AND PERSPECTIVES

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The paper provides the summary of foreign literature data on the organizational and methodological aspects of functioning of the bone marrow and hematopoietic stem cell donor registries, the issues of HLA typing, the technical algorithms for compatibility degree ranking. The changes in the citizens' motivations in response to the bone marrow donating program popularization are described, along with the features of arranging recruitment, approaches to determining the requirements for the registry population considering the multinationality and heterogeneity of ethnic composition, and the statistical approximation algorithms. Furthermore, attention is paid to the so-called specific aspects of the functioning of bone marrow and hematopoietic stem cell registries and biobanks. The latter is important in terms of ensuring national security, adaptation of the population to the effects of the disasters, emergencies, and terrorist attacks associated with the development of bone marrow syndrome in a large number of victims.

Keywords: registry, bone marrow, HLA, donors, typing, donor recruitment, transplants, acute radiation syndrome, NMDP, WMDA

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ГЛОБАЛЬНЫЕ И НАЦИОНАЛЬНЫЕ РЕГИСТРЫ ДОНОРОВ КОСТНОГО МОЗГА: ОПЫТ ИСПОЛЬЗОВАНИЯ, ОСНОВНЫЕ ТРУДНОСТИ И ПЕРСПЕКТИВЫ

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В статье обобщен ряд представленных в зарубежной литературе сведений, касающихся общих организационно-методических аспектов функционирования регистров доноров костного мозга и гемопоэтических стволовых клеток, проблематики HLA-типирования, технических алгоритмов ранжирования степени совместимости. Описаны изменения мотивационной сферы граждан в ответ на программы популяризации донорства костного мозга, особенности организации рекрутинга, подходы к определению требований к численности регистра с учетом многонациональности и неоднородности этнического состава и алгоритмы их статистической аппроксимации. Кроме того, уделено внимание так называемым специальным организационно-методическим аспектам функционирования регистров и биобанков костного мозга и гемопоэтических стволовых клеток. Последнее важно с точки зрения обеспечения национальной безопасности, адаптации населения к последствиям катастроф, чрезвычайных происшествий и террористических акций, сопровождающихся развитием у большого числа пострадавших костномозговой формы лучевой болезни.

Ключевые слова: регистр, костный мозг, HLA, доноры, типирование, рекрутинг доноров, трансплантации, лучевая болезнь, NMDP, WMDA

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To date, extensive experience of using the data acquisition and processing systems to facilitate the process of finding the HLA-matched biomaterial for transplantation have been accumulated in the world's healthcare practice. This technological category particularly includes registries of bone marrow (BM) and hematopoietic stem cell (HSC) donors designed to radically increase transplants access facility in terms of a broad range of diseases associated with hematopoietic system abnormalities.

In the context of the steadily increasing diversity of the registered HLA-associated alleles of potential donors, the increase in the likelihood of finding a compatible donor has been achieved. Such kind of circumstances can significantly improve the clinical outcomes of transplantation.

Though the registries of bone marrow donors emerged in different countries in a random-timing manner, we can say with reasonable confidence that currently a 40-year experience of their practical use has been accumulated globally. The wealth of knowledge, achievements, and various methodological approaches accumulated over such a long period could be of use for national medicine, considering the fact that the project to create the Federal Registry of BM and HSC Donors was launched in the RF in 2022. The aim of the paper is to summarize the data related to the organizational and methodological aspects of the register functioning, the issues of HLA typing, and a relationship with the sphere of national security. Certain technical information about the software and hardware arsenal used by the world's registries is important in terms of determining the current competitive position of our country in the field of the information technology support of bone marrow transplantation and innovative advancement reference points delineating.

Organizational and methodological component of foreign registry operation

The registry of bone marrow donors represents a multilevel complex hierarchical system of interaction between the computational algorithms, databases, and information flows from the users' workstations. The use of such systems ensures the coordinated work of diversified medical institutions, a considerable share of which provides highly specialized medical care and high-tech diagnosis. A significant proportion of the themes related to the work of such registries are focused specifically on the biomedical problems of hematology, transfusiology, transplantology, immunology, biotechnological features of determining the polynucleotide sequences, etc. However, the availability of sufficient quantities of high-quality donor material with the target properties and the possibility of its immediate use for transplantation always represent the key problem, no matter how completely all the specialized medical issues are resolved. Solving this kind of problem is related to the need for drafting and subsequent structuring of the organizational and methodological tasks implying accumulation of sufficient quantities of donors with various HLA phenotypes and ensuring the most effective preparation of biomaterial for timely transplantation.

Issues of forming and replenishing the donor pool. Role of motivation

Indeed, the issue of motivation and donors pool replenishment represents one of the most important and fundamental problems of all registries. The reason is that donating bone marrow is associated with several factors, which, at first glance, seem to be a formidable obstacle for involvement of

a large human population in voluntary medical activity of this type. First, donating is unpaid. Here it should be noted that, despite the fact that the global issue of medical transplantation commercialization should not be overlooked, the most important national registries forming the basis of the world's medical cooperation in this field work entirely on a gratis basis. Second, donating is associated with feeling uncomfortable and pain, even under anesthesia of any type. Third, there are no close family, friendly, or even social contacts between the donor and the potential recipient. According to the data provided by American authors, the National Marrow Donor Program (NMDP) founders' initial attempts to secure the reliable sources of funding for the wide propaganda of donating bone marrow met with serious resistance that was largely based on the above reasoning. However, in 1991, after using large federal funds for NMDP, the original skepticism dissipated quickly: in just 2 years the donor pool of the registry expanded from 250,000 to 1 million, reaching more than 6 million citizens by the year 2006. The fact of successful consolidation of public opinion around the valuable "altruistic" resource resulted in the need to increase the output, since, according to rough estimates, less than 5% of potential donors attracted to the registry would be de facto activated [1]. In this regard, it was proposed to actively engage registrants in recruitment of donors (by analogy with network marketing, MLM), participation in other medical and public health initiatives, and even in the direct financial support of those. The criticism of such initiatives was overcome by the fact that the registry members initially engaged within the framework of the request for a single donation later agreed to repeat the donation and participate in the other promising form of replenishing the pool of donor material for transplantation, the HSC apheresis associated with the completely different medical manipulations (injections of pharmacological agents followed by the prolonged peripheral venous catheterization for blood collection and reinfusion) [1].

Despite quite expansion of the NMDP registry and the lack of consensus on the method to determine its needed number of donors, the importance of various actions and initiatives to involve new participants on annual basis is emphasized by the American specialists. The reasons for that are the problem of "natural decline" in the number of NMDP donors occurring after reaching the age of 61 years and the negative correlation between the donor's length of stay in the registry and the likelihood of his/her successful activation. Based on the accumulated experience, the 4-year threshold of staying in the registry was determined as critical in terms of the sharp increase in the probability of the donor's refusal of activation [2], while it follows from the relatively early NMDP reports that about 30% of the registered donors who match the recipients based on HLA parameters turn out to be not available at the time of activation [3]. Moreover, in 2006, the share of Caucasian recipients, who had absolutely no HLA-matched donors, in the NMDP registry was 25% [1].

The major obstacles to increase the number of registry participants include high demand for funding: adding every 100,000 donors to the registry is associated with additional expenses of up to 10 million dollars [4]. To better illustrate the major changes associated with the multi-fold increase in the number of donors in the registry, it is appropriate to mention that at the dawn of its creation NMDP had only 200,000 donors and one full-time employee, while in 2008, when the number of donors reached 7 million, there were more than 600 employees, and the office area increased to 160,000 m² [5].

With regard to the high resource intensity of work on the creation of such registries it is reported that it is necessary to

partially redistribute the material burden, from state to private institutions engaged in charity activities. It is also proposed to work out the measures aimed at reducing the costs of filling the database of the registry donor pool. The potentially useful measures reported include the switch to collection of buccal epithelium biosamples (the method was introduced into practice of NMDP in 2006 [6]), reducing the costs of HLA typing, and improving performance of the recruitment centers [1].

The latter of the above mentioned approaches is being considered by foreign authors from both fundamental point of view involving the analysis of motivational and psychological features of influence on the future donor anurely organizational and methodological point of view confined to describing the features of selection and subsequent professional training of the recruiting staff. Within the framework of the first approach it is reasonable to note the papers focused on studying motivations for entering the registry. It has been found that the priorities and behavioral modes of potential donors represent a complex phenomenon. Furthermore, among factors contributing to making positive decision, altruistic personal traits and social responsibility are noted, while the opposite characteristics include cautious attitude towards healthcare system and adherence to religious values [7–9].

Conducting informational and educational events, as well as introduction of the popularization programs, is considered to be an effective method to deal with the psychosocial features that prevent donating [10–12].

In this context, the studies focused on determining the optimal methods for social communication are of great importance. Thus, the results of the experimental study aimed to compare the effectiveness of rational reasoning and emotion-oriented involvement in the social advertising about transplantation have shown that the emphasis placed on the sentimental component can to the greater extent increase both the likelihood of registration in NMDP and the likelihood of the appropriate information dissemination across family members and close friends of the new potential donor [13].

The practice of accelerated recruitment of the donor pool of the DKMS international registry Chilean branch involves simultaneous use of the whole range of online and offline communication channels, including the official website, information channels of social media, television, radio, press, and news aggregators. Furthermore, the emphasis was placed on the series of one-off actions aimed at helping the specific patient in need of unrelated transplantation. During such actions, which usually took one or two days and involved the patient's parents and friends, people, who were ready to donate bone marrow, were registered at local schools, sports clubs or community centers. As for 2022, a total of 695 such actions had been organized (among them 303 in 2022). The most successful offline event represented a three-day action organized in the cities of Santiago and Temuco, during which more than 6300 potential donors were recruited for the benefit of the 9-year-old female patient with leukemia. Since it was officially founded in February 2018, the registry managed to recruit about 170,000 people ready to donate [14].

The range of recruiting methods used by the Indian Genebandhu registry of bone marrow donors was significantly less diverse and comprehensive: motivational speaking in front of the audience, direct individual-oriented persuasion, hanging banners and posters were used. Furthermore, the registry managed to recruit 7682 potential donors in 2012–2018 [15].

The experience of arranging recruitment of one of the Russian local registries of bone marrow donors, Rosplasma, suggests reliance on the existing network of plasma centers and holding mass actions in educational institutions [16].

The studies of the most common causes of drop-out from the NMDP registry and non-confirmation of the previously declared consent when requested for transplantation revealed predominance of such factors, as changes in health status, discovery of the fact of inadequate clinical assessment at initial recruitment, incorrect registration of contact information, incomplete information about the upcoming procedures and possible complications, etc. [17]. Some authors believe that the category of adversely affecting factors also includes entering the registry together with the individual donating to certain patient (usually a relative) and making the decision for ethnical reasons [2]. The typical reasons of inability to activate potential donors from the Canadian registry include failure of attempts to get in touch using previously collected contact information, inability to donate due to personal reasons, such as interference with work or study, loss of motivation; in 1.8% of cases the registrants refused to specify their “no go” reasons [18].

As for the features of selection and subsequent professional training of the recruiting staff, it is reasonable to divide such specialists into three categories in ascending order of their competence levels: group leaders, professional and volunteer recruiters, in accordance with the World Marrow Donor Association (WMDA) guidelines. Among the skills and characterological profile elements essential for all categories without exception, the ability to build effective communication aimed at boosting recruitment, the ability to maintain and improve contacts with various categories of specialists and registry volunteers, personal empathy and high motivation are noted. It is also noteworthy that, according to the above WMDA document, such a rare option, as effective functioning in multidisciplinary environment, is a keystone trait of the professional recruiter to the registry.

Among the routine functional responsibilities of the specialists under consideration, assessment of the donor availability for activation is particularly emphasized, while among the most critical knowledge, the arguments in favor of the importance of the donor's life saving mission, donor validity criteria and rules for working with confidential information are highlighted [19].

Search algorithms and the likelihood of finding a matched donor

Another important aspect of the organizational and methodological component of the register activity is represented by the timely delivery of the donor material for transplantation, since the time allocated for the search, transportation, diagnostic, legal, financial, and other activities preceding the final phase of hematopoietic failure treatment is usually extremely limited. The NMDP practice suggests partial unification of the search algorithms and strong dependence of the latter on the opinions of the registry physicians and coordination staff. Statistical studies have shown that the approach, in which the first search phase is guided by the hardware algorithm (using the electronic computational system to form the most promising donor-recipient pairs), but the final decision is made by the patient's physicians, is the most popular. The second most important one is represented by meetings of commissions and round tables (meeting of experts presumably using different variants of decision making procedures), while reliance primarily on the hardware algorithm ranks only third. Traxis, NMDP search strategy advice/HLA consultation, HapLogic donor, and CBU match prediction are the most commonly used information resources used for search (in descending order of popularity). Among the main

tools aimed at increasing efficacy of the search made for the benefit of certain patient under time pressure, the following are reported (in descending order of popularity): simultaneous activation and management of several donors, priority setting by the transplantation center coordinator when examining the donors, driving the donor to transplantation in parallel with the process of confirmation typing and limiting the search pool to the donors, the last contact with whom was made recently.

When it is impossible to find the 8/8 HLA-matched donors (match by four most important HLA-associated nucleotide sequences of both chromosomes 6), the strategies related to the search for haploidentical donors, selection of cord blood or even activation of a partially mismatched 7/8 HLA donor are used (in descending order of popularity).

The use of the whole combination of the above measures results in the fact that nowadays inability to find an appropriate donor is not the most serious obstacle on the way to timely transplantation. The far more significant factors include inability of the third-party registry to meet the schedule of biomaterial collection, problems related to acquisition of the typing results, and insurance problems [20].

Despite the perfection and diversity of algorithms for finding matched donors and the steady upward trend in the number of world registries, the issue of their completeness is especially pressing in the context of multinational and ethnically diverse states, where rare variants of HLA phenotypes constitute a significant part of the common pool and turn out to be associated with the closed populations.

A vivid reverse illustration is such country with low HLA diversity, as Japan, where the likelihood of match by antigens A, B, C, and DR of approximately 95% was achieved after the Japan Marrow Donor Program (JMDP) had formed a three hundred thousand pool of potential donors [21].

In Saudi Arabia, the likelihood of finding a 10/10 matched (match by five most important HLA-associated nucleotide sequences of both chromosomes 6) HSC donor is about 50%, given there is a million donors in the registry [22].

A slightly different situation is observed in Israel, where the degree of ethnic and subethnic diversity has a great impact on the likelihood of finding donors with a high degree of compatibility. As for 2017, bioinformatics modeling showed that this parameter was 40–55% depending on the fact of belonging to particular ethnic or subethnic subgroup, and its growth of about 1% per year was predicted based on the registry filling rate [23].

However, the more recent findings suggest that unique alleles have been reported in the sample of 223,960 potential donors added to the Israeli registry in 2018–2021. This fact may indicate that the degree of HLA diversity in the Israeli cohort is still poorly understood and probably should be adjusted upward, which can affect approximation of the likelihood of finding the matched donors [24].

India represents one of the most vivid illustrations of registries filing issues caused by the ethnic diversity of the population. This country is home to more than 300 ethnic groups speaking 438 languages, and the pools of five main registries of bone marrow donors are as follows: DKMS Registry (21,695 donors), Be The Cure Registry-Jeevan Foundation (6449 donors), Datri Blood Stem Cells Registry (367,561 donors), GeneBandhu (7991 donors), and Marrow Donor Registry India (MDRI) (35,768 donors). In this case, the likelihood of finding an appropriate variant for transplantation, even without considering the requirements for high HLA typing resolution, is below 20%, since more than a third of HLA types are unique (the so-called singletons) [22]. Furthermore, it should

be emphasized that the probability values provided for India are empirical, while these provided for KSA (Kingdom of Saudi Arabia) are estimates (prognostic values). The key parameter that opens up the possibility of this kind of approximation and, as a consequence, the possibility of estimating the target values of register fullness, is the measure of genetic HLA diversity of the population, which, given practical impossibility of typing 100% of all individuals in the population, also requires statistical prediction. The probabilistic approximation of such type becomes available due to extrapolation to the whole population of HLA typing data of the registry donor pool. The lack of unified typing methods is the main difficulty preventing the mentioned procedure in foreign countries, which results in eclectic picture of HLA data with different resolution accumulated over the decades, along with high abundance of unique alleles (high percentage of singletons). The most obvious and simplest solution to the problem of consistency of information about HLA genotypes, reduction of all data to the lowest resolution of all represented in the system, leads to the significant decrease in the allele diversity recording performance, that is why it has been proposed to use the statistical algorithms capable of operating in the context of samples that are mismatched based on the specified criterion [25]. As for overcoming the second obstacle, it is necessary to note the statistical developments in adaptation of the expectation-maximization algorithms to the distributions characterized by the so-called heavy tails. Application of the algorithm to the data of donors from the US national registry has in particular shown that 44.65% of the haplotypes of Caucasian Americans are singletons, i.e. are unique. Furthermore, the share of representation of the haplotype variant types in the register relative to their total number among Caucasian citizens of the United States is only 23.45%. However, the 6.59 million pool of donors is enough to ensure 99.4% population coverage due to the fact that 90% of Caucasian Americans have one of the common haplotypes (4.5% of cases) [26].

Thus, the targets of the number of donors are calculated using mathematical modeling, the results of which depend heavily on the characteristics of input data, specifically HLA typing data. These characteristics may change depending on the method of reduction to one or another standard and, therefore, affect the mathematical model performance. Hence, we can conclude that the issues of filling the registry and calculating the target values of this parameter are rather closely related to the issues of the applied HLA typing methods' standardization.

HLA typing in activities of the world's registries

Currently, there are no data on using the standardized approaches to HLA typing in the international peer-reviewed literature. The multivariate nature of the HLA genotype determination procedures persists in several areas at once, which merits special consideration.

Completeness of information about the nucleotide sequences of genes encoding the major histocompatibility complex (MHC) proteins obtained during HLA typing is the most multivariate. The today's typing techniques make it possible to acquire information about the following:

- nucleotide sequences encoding the most significant regions of the antigen-recognition domains of MHC proteins;
- complete nucleotide sequences encoding the antigen-recognition domains;
- complete (excluding synonymous variants) nucleotide sequences of the exons encoding the entire structure of MHC proteins;

- complete (including synonymous variants) nucleotide sequences of the exons encoding the entire structure of MHC proteins;

- complete (including synonymous variants) nucleotide sequences of the exons encoding the entire structure of MHC proteins and complete nucleotide sequences of introns in the MHC genes;

- complete (including synonymous variants) nucleotide sequences of the exons encoding the entire structure of MHC proteins and complete nucleotide sequences of introns in the MHC genes, along with information about the expression levels.

The available data on the ongoing research developments aimed at combining the data on the nucleotide sequences of HLA genes with different integrity levels (resolution) and the structure of international HLA nomenclature are indirect evidence of the fact that there are currently typing data of almost all the above resolution types in the databases of world's registries [27, 28]. The typing data with different resolution are sometimes found within the same registry. An example could be the international DKMS registry (Germany, UK, Chile, Poland, South Africa, USA), where, despite the 6-year experience of typing performed based on six conventional HLA genes, in 2019 the German data set was still characterized by the presence of 100,000 donors typed by two HLA genes only [29].

In the Italian registry of bone marrow donors (as for 2017), there is a practice of using the so-called “primary requests” when performing the search for donors, in which the fact of match is determined based on the low-resolution HLA typing data. This procedure was recognized as useful in terms of accelerating the search for matched donors [30].

The NMDP procedures provide for the possibility of limiting to the first two of the completeness levels of information about the MHC genes presented in the above list at the time of entering the registry, however, at the time of activation it is necessary to perform typing aimed at determining the complete nucleotide sequences of exons (points 3–4), which corresponds to the term “high resolution” used in foreign procedures [31]. The list of the typed major histocompatibility complex protein molecules is also multivariate. For example, since the NMDP creation, the initial requirements specified only the HLA-A, HLA-B, and DR receptors as mandatory. By 2005, the requirement of additional HLA-C typing was added, and therefore the term 8/8 MUD (Matched Unrelated Donor) indicating the appropriate match standard came into practical use. The convincing data on the importance of such receptors as DP, DQ started to emerge over time, and the 10/10 MUD was gradually introduced into practice [32].

The designated areas of procedures and requirements belong to the category of typing outputs, while the technological process of acquiring those is also multivariate. Currently, several main types of technologies that can be used for HLA typing are distinguished: PCR-SSP (polymerase chain reaction with sequence-specific primers), PCR-SSOP (polymerase chain reaction with sequence-specific oligonucleotides probes), SBT (sequencing-based typing), next-generation SBT [33–37]. Furthermore, the last technologies from this list enable acquisition of the most complete genotyping results, while the PCR-SSP and PCR-SSOP techniques confine the resulting dataset to information about the sequences of antigen-binding regions; these are often linked to the catalogues of the abundant and well documented CWD alleles. The latter are designed to partially compensate the lack of information about the nucleotide structure of HLA macromolecules (insufficient resolution) and are used as the templates for targeted search when conducting PCR [38].

Today, thanks to the efforts of such organizations, as the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI CWD), and China Marrow Donor Program, the CWD catalogues are maintained in the USA, European Union, and China [37–39].

Specific aspects of the Western BM and HSC registry functioning. Ensuring national security

All the organizational and methodological aspects of the work of world's registries of bone marrow and HSC donors considered so far can be classified as common. The reason is that these are realized within the framework of routine functioning and are not exclusive. However, the literature data suggest that the so-called specific aspects of the registry functioning (procedures and programs of functioning in emergency situations, such as disasters of all kinds) are also subjected to methodological workout. In 2012, the guidelines for international members of the organization on the implementation of the plan for countering natural, industrial or other man-made emergencies was issued under the aegis of WMDA [40].

The document outlines the range of main directions for organizing counteraction to the negative consequences of an emergency that has already occurred or is unfolding. It is noteworthy that the first paragraph is of general nature and implies the registry system response to the destructive processes and events that are not directly related to the registry function impairment. Given that such definition opens the door for the extremely broad interpretation, the assumption about the document authors' effort to lay foundation for the development of procedures for providing large-scale assistance to the population using the registry resources seems to be logical enough. The situation of mass radiation exposure to the doses of 5–10 Gy, when bone marrow transplantation is a life saving-procedure, represents an example of the increased demand for the donor potential of the bone marrow registries in the context of exposure to adverse factors and disasters. The strategic plan described in the document, in which the first paragraph shows the importance of forming the system for priority workout of the rating of potential requests for transplantation in crisis conditions, represents the potential additional evidence suggesting the possibility of working out the scenarios for countering radiation damage. Theoretically, prioritization of this kind can be very important under conditions of mass radiation exposure due to inability to simultaneously satisfy many potential recipients and the need to make tough decisions about the involvement of donor resources in one or another area.

Furthermore, it is necessary to mention that such an aspect directly related to registries, as the possibility of creating the BM and HSC banks also intended for autotransplantation, was discussed in the media with regard to the Fukushima nuclear accident. According to the report issued by Scienceinsider, the group of Japanese medical experts, including Tetsuya Tanimoto being a representative of the Japanese Cancer Association, addressed a letter to The Lancet journal on April 15, 2011, in which it expressed the need to organize a HSC bank for the plant employees [41]. The authors believe that this measure is intended to reduce negative effects of possible exposure to high radiation doses. To confirm the authors' opinion, Scienceinsider cites the words of Nelson Chao (Duke University in Durham, North Carolina), the expert in transplantation, who declares undoubted benefits of such measures for overcoming the effects of the radiation exposure associated with cancer treatment.

Some interesting facts related to the very moment of founding the US national registry of bone marrow donors are indirect evidence of the global registries' adaptation to the scenarios of nuclear disasters. Actually, in 1984, Al Gore, the congressman (who later became the US vice president) failed to overcome the resistance of the White House considering this initiative as untimely, despite huge personal enthusiasm and extensive political power. Support could not be achieved even during a special coordination meeting organized under the auspices of the NIH, and the concept of the registry was realized only in 1986 due to the fact that the US Navy was granted 1.2 million dollars. It is interesting that Captain Robert J. Hartzmann, head of the naval transplantation registry, was aware of all the nuances of financial arrangements [42]. Given the strategic importance of using nuclear power plants on the war ships constituting the basis of the US Navy striking force, this fact can show that there are specific reasons for creation of the world's largest BM and HSC registry, including that related to overcoming the effects of the personnel radiation exposure.

CONCLUSION

Thus, the review discusses the literature data on the long-term worldwide experience of using the bone marrow and HSC registries focused on the common and specific organizational and methodological aspects of the registry functioning. These data have been critically reviewed; the data credibility and practical value are beyond doubt.

In particular, in the RF, information about the citizens' high responsiveness to the bone marrow donating popularization programs, the features of arranging recruitment, the requirements for the registry population considering the multinationality and heterogeneity of ethnic composition, and

the algorithms of its statistical approximation are of great interest in terms of implementation of such information systems. In the context of technological support, the data on the diversity of algorithms to search for matched donors, including those targeted to the using of the alternative transplantation material sources, such as Cord Blood Unit и Peripheral Blood Stem Cells, attract attention, along with the fact of the global registries' adaptation to the diverse HLA typing methods. The data on the potential relationship between the BM and HSC registries and the problem of ensuring national security, are of special importance, including in the context of protecting the population against the effects of the disasters, emergencies, and terrorist attacks associated with the development of bone marrow syndrome in victims. The fact of scientific arguments in favor of creating the BM and HSC biobanks for populations at high risk in terms of the radiation exposure factor deserves special mention in this regard.

The relevance and practical significance of the data provided in the review are confirmed by the fact of underrepresentation of the themes related to the activities of the national registries of bone marrow donors, specifically the Federal Registry of Bone Marrow and HSC Donors, in the Russian scientific literature. Currently, such papers are focused mainly on the legal aspects of the registries' activity [43, 44], reiteration of the need to its creation [45], and practical results of the work of only one registry, the Rosplasma Center of FMBA of Russia [16].

Given the above, it is reasonable to put forward a hypothesis that further accumulation of the pool of domestic papers focused on the Russian experience in this sphere will make it possible to take full advantage of the foreign research data provided in the review as the basis for comparison and arrangement of the productive debate about the optimal ways to develop the Federal Registry of Bone Marrow and HSC Donors.

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