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Notes on Visit to Minsk (11/8-11/18, 1995) and Follow-up in Geneva (11/18-11/24/95)

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INTRODUCTION

This visit to Minsk had been long delayed since the previous visit in May, pending clarification of the administration of the BelAm project. Dr Wachholz and Dr Mincey had succeeded in getting the Minister of Health to accept the project as a major undertaking of her office. She had appointed Dr Krisenko, a deputy Minister, as Director of the BelAm Project. Dr Stozharov, director of the Institute of Radiation Medicine, and Dr Rzheutski, director of the Minsk National Dispensary, were appointed as his deputies for non-clinical and clinical operations, respectively.

The visit was made in the company of Dr Jacob Robbins and Dr A B Brill, both members of the NCI working group on the Chernobyl thyroid studies. In Geneva, where I met Dr Wachholz, we also had Drs Anspaugh, Becker, Shore, and Van Middlesworth, other members of the working group. Among those with whom we interacted in Minsk were: Drs Krisenko, Stozharov, Rzheutski, Danilova, Drozd, Astakhova, Polanskaya, Orlov, Minenko, Litvinova, Petrenko, Silich, and Voronetsky as well as Mr Arthur Kuvshinnikov, head of the Data Coordinating Center for the project.

The notes are organized by topic, as follows:

ESTABLISHING THE COHORT. The scientific protocol calls for a cohort of 15,000 subjects with 1986 thyroid measurements, all those with estimated doses of 1 Gy or more (about 5K), about 6 K with estimated doses of 0.3 to .9 Gy, and about 4 K with estimated doses below 0.3 Gy. We could find no plan to create the cohort despite the pressure being put on having a pilot run of the clinical screening examination in December, Discussion revealed dissension between the Epi group of Dr Voronetsky and the DCC (Mr Kuvshinnikov), and between the Epi Group and the Minsk dosimetry group (Dr Minenko). A conference was arranged at which Dr Minenko revealed his preference for having the Moscow dosimetry group, rather than his Minsk dosimetry group, provide the computer file of usable measurements from which the Epi group and the DCC would seek to obtain up-to-date addresses. This position was later confirmed by Dr Stozharov who promised to call all the parties together in order to settle the responsibility for providing the necessary file. Meanwhile I learned from Dr Bouville that the Moscow dosimetry group had already provided Minsk with the file that was needed to start the work of locating subjects, and that the file consisted of 39 K, not 28 K, as we had been told. He also indicated

that the Moscow group had provided all the information it had on these 39 K potential subjects; there was nothing more it could do. Mr Kuvshinnikov had a copy of the file; it was in a single format ready to be linked with registries containing addresses. He verified the count and indicated that there were 6,200 with estimated doses of 1 Gy or more. The file was ready to be used.

In a discussion with Dr Voronetsky and Mr Kuvshinnikov, which appeared to be quite amicable, it was possible to outline an acceptable strategy for obtaining the necessary addresses, as follows: (1) The Epi group would arrange access to computer files that the DCC would collate with the measurement file in order to transfer address and other useful information; (2) the DCC would perform the necessary record linkage by computer, transfer the desired information, and begin to fill up the cohort as outlined in the protocol; and (3) the Epi group would arrange access to manual files where there were no computer files, solicit local help in manual record linkage, and transfer desired information to linked records in the measurement file, further augmenting the cohort. Emphasis would be placed on the early selection of 2-3 K subjects for the Minsk Dispensary to work with, once the screening examination, the data flow, and the central lab were operational. It was said that the computer file of the Minsk Dispensary itself plus the WHO file of about 15 K subjects seen in the past two years would suffice to start the routine screening operation in the Minsk Dispensary within the next 2-3 months. A first trial run had been set for December.

A memorandum (see attachment 1) was prepared for Dr Krisenko stressing (1) the urgency of the need to start building the cohort, (2) the availability in Minsk of the file needed to start the work, and (3) the feasibility of a division of labor between the DCC and the Epi group.

The probable insufficiency of the Moscow file of thyroid measurements was clearly foreshadowed by the results of the effort to locate the representative 600 subjects in that file (cf below).

PILOT WORK ON THE SAMPLE 600 FROM THE MOSCOW MEASUREMENT FILE In 1994, on the basis of a memorandum prepared in cooperation with the Minsk staff, the Minsk dosimetry group had selected 600 subjects from the measurement file, 200 from among those with doses estimated to exceed 1 Gy, 200 at 0.3 to 0.9 Gy, and 200 <0.3 Gy. Dr Voronetsky had essentially completed his work by the time of the May visit, and his results are given in attachment 2. At the Nov visit he had not yet written up the work and felt that there was little more he could do. He had, however, tapped the Gomel Oblast file of the Ministry of Internal Affairs but had not been able to obtain access to these files in the Minsk and Mogilev Oblasts. An implication of his work was that perhaps 56 percent of the 6,200 with doses of 1 Gy or more might be located for the cohort, well under the 5 K specified in Dr Shore's calculations for the

protocol. Dr Shore and I had drafted a proposal to revise the protocol by supplementing the Moscow file with part of the recently discovered Brest file, subject to a positive evaluation of the latter by the dosimetry groups. A copy of that proposal is attachment 3. Dr Voronetsky, in May, had been in favor the procedure outlined for modifying the protocol, but the draft we prepared in August had failed to obtain his approval. In our November talks he indicted that the Brest file would not be available for the BelAm project, that there were other uses for it. (See Brest File, below).

Dr Voronetsky provided very useful maps that are reproduced as attachments 4 and 5: 4 gives the distribution by district of the measurements made in 1986, and 5 the distribution by district and city of the addresses he had located among the test sample of 600. Those results suggested that a cohort of 15 K might not provide more than 1,000 subjects within easy reach of the Minsk Dispensary, and that it was imperative to get the planned Gomel center organized soon, certainly within 1996.

A later conversation with Dr Krisenko in Geneva suggested that he was prepared to open doors to files unavailable to Dr Voronetsky, files that might substantially increase the 56 percent result Dr Voronetsky had obtained with the test sample. At that time I emphasized to Dr Orlov, who had accompanied Dr Krisenko to Geneva and served as his interpreter in our conversations with him, the importance of first working the test file of 600 against any new resources Dr Krisenko was able to provide. Also, until Dr Voronetsky writes up his experience with the test sample it will not be clear to us how thorough the search actually was. He did indicate that some of the work was done for him by local authorities, e.g., in Gomel.

When I suggested that Dr Voronetsky solicit the help of those located, asking for information on those not located among those measured in the same area as those he had located, Dr Voronetsky replied that he had already tried this but with no success. Those located seemed not to know the whereabouts of those not located. This may be because he located mainly people who had remained in the area where they had been measured, while those not located had moved away.

THE CASE-CONTROL PAPER Before leaving Rockville Dr Robbins, Dr Waclawiw, and I had prepared, and forwarded to WHO under date of 6 November, the text of the paper for WHO. We had also prepared transparencies for Dr Astakhova to use in her presentation. I took this material on diskette for possible modification in Minsk following consultation with Dr Astakhova. Dr Polanskaya kindly arranged for Dr Robbins and myself to meet with Dr Astakhova, herself, Dr Moshchik, and Dr A Nalivko, a co-author, in Dr Astakhova's new offices in Minsk (Tel 31-3346). We discovered some errors in names, an omission in the acknowledgement, and a

distortion in the printing of one table for the overhead. Dr Astakhova also asked for one new table. Most important was Dr Orlov's introduction of a report by Drs Ivanov, Tsyb et al on a case-control study of 17 cases of thyroid cancer and 107 controls in Russia. They had individual doses and seemed able to show a significant relation between cancer status and dose. We were able to include this in the discussion section of the paper and to add it to the list of references. With the diskettes available for the text and the transparencies, it was possible to make the necessary changes and to provide Dr Astakhova with a corrected text (14 November) and a diskette for WHO, as well as the transparencies needed for her presentation. Told she had only 10 minutes for each of two papers to be presented in "parallel sessions" outside of the main session, she elected to take 25 minutes for both for a presentation in a main session, where she did well enough, even though she had to hurry through the material more rapidly than one would have liked. There was only one question, apparently related to her second paper.

THE DATA COORDINATING CENTER We found the office of the DCC crowded with new furniture and equipment partly intended for the Project Office across the hall, still under preparation. I found the DCC office pleasant and functional. It is a good corner room. There is a long table suitable for perhaps 16 people where Dr Krisenko presently holds weekly staff meetings. Mt Kuvshinnikov is very much in command, although organizationally he is under Dr Voronetsky and perhaps will be until the DCC has enough personnel (perhaps 7) to stand alone as a unit. Mt Kuvshinnikov has one assistant, Nadia, and Dr Mincey also uses the DCC as his office. There are 3 PC's set up, a printer serving all of them, facilities for copying and for sending messages by FAX. The copier lacks a sorter and must be fed in single sheets or in book mode. Much of the communication centered here is by e-mail. We were told that the $400 provided for e-mail expenses by LLNL in September was almost exhausted and that the fund could be replenished only by LLNL personnel bringing more cash, perhaps in March when Sheila was expected, unless Dr Anspaugh could be in Minsk sooner.

Mr Kuvshinnikov had prepared a flow chart of the procedural steps, and a copy of this is attachment 6. I thought it would be well to add linkages with the Chernobyl Registry and the Cancer Registry for ongoing efforts to locate subjects who moved and to check on the completeness of ascertainment of thyroid cancer.

We early found Dr Voronetsky desirous of a major, perhaps exclusive, role in the creation of the cohort, but the discussion already referred to above appeared to satisfy him as to the necessity for a division of labor between Epi and the DCC. He said he had felt left out of the discussions with Dr Mitchell when the latter was in Minsk in August.

In staff meetings and in a review session at the Minsk

Dispensary, Mr Kuvshinnikov demonstrated that he had the best understanding of the screening process as well as the data flow, and was very articulate and precise. He is perhaps the most valuable single member of the project staff. His relation with Dr Mincey seems quite easy and effective. He seems quite dedicated to the project and to work very hard at it. With his knowledge and equipment, and his friendly nature, however, his aid is solicited by all and sundry for manifold tasks, many of which do not relate to the BelAm project. Dr Mincey commented on this and thought he could do something about it.

Dr Robbins raised the issue of data analysis as a possible function of the DCC. This will need serious consideration soon. My first thought was to train a staff member in both epi and statistics to perform functions in both areas, but its feasibility rests on the availability of a suitable trainee and money for project salaries.

DR KRISENKO'S STAFF MEETINGS There were two while we were in Minsk, both devoted mainly to preparations for a pilot run of the screening program in the Minsk Dispensary during December. These were held in the DCC and attended by Dr Rzheutski (one), Dr Stozharov (one), Dr Orlov, Dr Drozd, Dr Danilova, Mr Kushinnikov, Dr Petrenko, Dr Litvinova (endocrinologist at the Dispensary), Dr Silich, Dr Voronetsky, Dr Minenko, Dr Mincey, and Mr Sviatelik, as well as the US visitors. Each element of the screening program was reviewed with those responsible and preparations for the pilot run discussed in terms of preparedness. Dr Krisenko seemed satisfied that the pilot run could be made in the period 11-15 December, but Dr Mincey, better acquainted with the details and their significance, said privately that it probably would be January before the run could be made. Subjects of the cohort would not be involved, but patients at the Dispensary available 11-15 December would be pressed into service. The interview would not be ready, nor would the DCC have the necessary software for a full operation. But all clinical and lab work would be done, and the study forms would be filled in.

The Toshiba US machine arrived while we were in Minsk, and Dr Brill brought some new software related to its use. Mr Kuvshinnikov, who was trained in electronics in the Soviet Army, proved adept at installing the new software with Dr Brill's help.

Dr Drozd had some problems with the US form that led to discussions with Dr Brill and some revisions in the form.

We discussed certification briefly and I was pleased to see that the idea seemed to be acceptable to the staff and to Dr Krisenko.

Arrangements were made to introduce a professor of psychology who might work on the design and testing of the initial interview.

Dr Krisenko had evidently taken a hand in this. Dr Minenko made it clear that he was in no position to provide personnel as interviewers.

In the second staff meeting on 15 November Dr Krisenko again reviewed preparations for the pilot screening with each staff member. Although problems were cited, e.g., bar-code labels were not ready, several forms were being changed, and some further training was needed, Dr Krisenko decided to keep the pressure on and retained the 11-15 December dates; there was no objection. Hope was expressed that Dr Robbins could be present and he, in turn, indicated that it might be possible.

It was during the above discussion that Dr Drozd mentioned that referrals to the Clinic for diagnosis might run about 4 percent, an important number that needs to be established from the first thousand or so of the screenees.

Dr Krisenko noted that we should be ready with cohort subjects after the pilot run and asked whose job it was to establish the cohort. Unfortunately the subject was not pressed at that time.

D Krisenko's objective is to meet every Thursday.

ORGANIZATION A very preliminary organization chart is attachment 7. It merely lists the various groups that have been recognized and their leaders. We were pleased to learn that Dr Danilova, a lady with a pleasant personality and whose English is excellent, would be the senior and supervising endocrinologist, and Dr Drozd her counterpart for US, although both are attached to the Aksakovtchina. Presumably they would also be responsible for handling referrals from screening sent there for diagnostic work-up. Their authority would extend to Gomel and to certification. Dr Danilova mentioned that she was prepared to go there for as long as two weeks at a time. She is already a consultant to the Minsk Dispensary.

In discussions at the Minsk Dispensary we learned that there might be an occasional subject who should have an immediate biopsy, for which the Dispensary is equipped. Dr Danilova would perform the biopsy there. Referral might then take place to Dr Demidchik without the subject ever being seen at the Clinic. There might be a problem with the paperwork in such circumstances unless special care was taken.

We received warnings, hard to evaluate, that Dr Stozharov might not be an effective leader of the non-clinical teams under his control.

MANUAL AND FORMS We brought copies of the latest (3 November) draft of the Manual prepared by Westat. In the first staff meeting I suggested to Dr Krisenko that an effort be made to update the

Russian translation of the Manual and that Dr Orlov be given this important responsibility on a continuing basis. In a private conversation Dr Orlov indicated that he was willing to do this, but by departure time we had not heard that the assignment had been made.

Dr Robbins provided some changes in text and in forms that will be sent to Minsk and to Westat. Dr Brill and Dr Drozd revised the US form. DR Mincey was re-working the laboratory forms.

All the evidence indicated that the Manual was well received by the staff and that changes would be made as experience dictated. Gomel representatives visiting Minsk received copies of the protocol and the 1994 version of the Manual in Russian.

There may be more fine-tuning of the indications for biopsy, as Dr Drozd reminded us that the US examination would find apparent nodules that could not be palpated. Dr Drozd wants more explicit provision for measuring gland volume and for recording this information on the US form. She was also concerned that the US examiner have available any information he would need for recommending referral (a function of the endocrinologist after consultation with the US specialist).

The most significant problem encountered with the Manual and the form revolved around (1) notification of the family as to the results of screening, and (2) the need for a final summary that would include information on the final diagnostic workup and any surgery and tissue diagnosis after the screening had been accomplished. We finally settled on a final screening report plus a final diagnostic report. This involves changes in the endocrinologist's preliminary and final screening forms plus the development of 2 new forms recording the results of the FNA and any pathology information following surgery. Parathyroid pathology should also be provided for.

It was agreed that the diagrams of the gland on the US and palpation forms should be better coordinated, and that better provision should be made for attaching thermal prints to the US form and perhaps the endocrinologist's final screening report.

We visualized a screening report for the family that would lack any explicit suggestion of cancer.

We discussed the need for instructions on the forms, simple things like their routing as well as definitions, etc. We merely acknowledged the need for such instructions without drafting any at that time.

In Geneva I learned that Dr Tronko had taken up with Dr Krisenko the question of access to the BelAm study forms for the thyroid study. This should have paved the way for their transmittal

to Kiev.

THE INITIAL INTERVIEW Negotiations are under way with Professor Sekun, a psychologist in the Institute of Sociology of the Academy of Science. to develop, test, and teach the use of, an appropriate initial interview. He is chief of a Scientific Program on the Social and Psychological Rehabilitation of Chernobyl victims, and chief of a department in his Institute, an experienced investigator using interview techniques. He had not been well briefed on our task and rocked with laughter on learning that we mainly wanted a nutritional history for the first few weeks after the accident. He was skeptical of one's ability to obtain reliable histories and inclined toward a research approach before attempting to design an interview. He seemed interested and competent to us. Can Dr Krisenko afford him?

GOMEL Soon after arrival we were told that arrangements had been made for an endocrinologist and an ultrasonographer in Gomel to visit the Minsk National Dispensary for three days of consultation. We waited most of the first day before learning of a train accident that had delayed them. The waiting time was well used, however, in reviewing the steps in the screening examination and our state of readiness, with Mr Kuvshinnikov providing the structure for the discussion.

We learned that the director of the Gomel dispensary had died very recently from complications of medullary thyroid cancer operated on two years before.

As noted above, it is clear that steps must be taken promptly to establish a center in Gomel. The representatives from Gomel were said to be amenable to the procedures of the study. I did not meet with them. We were told that Minsk would control Gomel through Dr Rzheutski administratively, with Drs Danilova and Drozd supervising endocrinology and ultrasound. The central laboratory in Minsk would receive blood and urine specimens from Gomel, and Gomel would follow the procedures established by the DCC. Referrals would be to Aksakovtchina. While Minsk is a national dispensary, Gomel is an oblast dispensary.

FINANCIAL SUPPORT OF THE BELAM PROJECT Dr Stozharov informed us that the Ministry of Chernobyl had provided some funds for the BelAm project in 1995, but that the Deputy Minister, in a statement to the press, had indicated that such support would be less, or zero, in 1996. Dr Voronetsky complained that Dr Stozharov could not get an understanding on money from the Ministry of Health.

Dr Robbins and I spent some time trying to put together the basis for a proposal (from Belarus) to LLNL for salary support. The guidelines for us called for:

(1) Breaking up the work of the project into discrete tasks

(2) Detailing the work to be performed under each task
(3) Estimating the personnel requirements for each task
(4) Indicating what personnel, or what units, would be involved in each task

We prepared the attached list (attachment 8) for Dr Mincey who modified and extended it as a document for Dr Wachholz. Both documents were used in discussions with Dr Krisenko in Geneva, and I spent some time with Dr Orlov explaining the LLNL contracting process as I understood it.

It remains to be seen whether DOE or LLNL will actually negotiate the necessary contract(s), and how soon negotiations can start. Dr Anspaugh informed us in Geneva that LLNL could not contract with the Ministry of Health but could with its Institute of Radiation Medicine and the Minsk National Dispensary. He thought DOE Hq could write a contract with the Ministry but this might take longer than would be the case if LLNL wrote the contracts.

In Minsk I again had the feeling that US financial support was needed soon if the project was not to collapse. It is unfortunate that we seem to have no mechanism for providing "start-up" money, and that Belarus can be paid only on the basis of work already accomplished.

Dr Krisenko had a private meeting with Mr Hawkins and Dr Gallin of DOE that none of the NCI group attended. This was planned as an effort to avoid any misunderstanding that might come from Mr Hawkins' address a few hours later. Some aspects of that talk could be taken to imply that DOE would not be in a position to provide full funding for the project.

THE BREST FILE As reported earlier, Dr Voronetsky had obtained the original notebooks on the extensive direct thyroid measurements in Brest, and in May discussed the use of this file to supplement the Moscow file in creating the cohort for the BelAm project. Some part of this file (kept in the safe in his office) had been made available to dosimetrists in Moscow and Minsk. It was said that their evaluations differed, and that their dose estimates differed by a factor of three.

My understanding from Dr Bouville is that, in September, all three dosimetry groups asked Dr Voronetsky for access to the notebooks for more serious study but that, thus far, this request had not been granted. He also indicated that the evaluation made by the dosimetry groups had been too preliminary to warrant a decision on the acceptability of the Brest file for the BelAm project.

Dr Robbins and I had three conversations with Dr Voronetsky about the Brest file. In brief: (1) he first indicated that we could not use the Brest file for the BelAm project: (2) he next said that he and Dr Stozharov had changed their minds and that the

Brest file cold be used in the Belam Project, and he proposed an innovative approach that would require an extensive change in the protocol; and (3) in his last conversation he reverted to his original position, which he said he shared with Dr Stozharov.

Dr Voronetsky has a 2,500 person cohort under study in Brest, with two-year funding from the Ministry of Chernobyl. I mentioned to him the possibility of a dual use of the Brest subjects in his study and in the BelAm project, with sharing of screening and diagnostic information on subjects common to both projects and provision of dose information for his purposes. He did not seem impressed.

Dr Voronetsky's idea, proposed in the second meeting on the Brest file, consisted of the following:

Minsk: Keep the central lab and eliminate all clinical screening

Gomel: Establish one team for screening in the dispensary most of the year; in the summers it could operate as a mobile team.

Brest: Establish two fixed screening centers in hospitals in eastern Brest.

This plan was given in confidence with the understanding that it would be shared with the US side only, a condition we accepted and respected. We told him it was a creative idea and urged him to write it up; he said he would do so by 15 December. The justification for the plan seemed to be:

(1) His work with the 600 test sample suggests that Minsk is not an efficient center, that effort must be concentrated in Gomel;
(2) He can locate only 56 percent of subjects in the Moscow file
(3) The Moscow file is too small in light of (2)
(4) The Brest subjects can be located at a high rate; and
(5) As between extending the Moscow file with subjects with passport doses, and supplementing it with the Brest file, the latter would be far superior.

Dr Voronetsky claimed to have talked with the physician in charge of the Stolin district and to have found him interested and believing in its feasibility.

In one of our conversations Dr Voronetsky expressed his extreme displeasure with the Minsk dosimetry group on the basis of a recent approach by Dr Drozdovich for information on the Brest file to be included in a paper the dosimetry groups were presenting shortly at a meeting in Germany. He called the approach unethical and was very emotional about it. I offered to discuss the subject with Dr Drozdovich and he accepted the suggestion. Nothing came of this, however, as Dr Drozdovich indicated that Dr Voronetsky's name had been put on the paper already, and that it would not be

possible to raise the money for him to attend the meeting in Germany, the registration fee alone being 700 DM.

IN UTERO SUBJECTS The BelAm protocol calls for inclusion of the in utero exposed whose mothers had direct thyroid measurements in 1986. There are other interests in this material. The WHO has a study of neurological effects of the accident, and Dr Voronetsky described a sample of 1,800 created by professor Karanov of the Medical Institute for Psychiatry who is working with the WHO group. Dr Voronetsky himself has a sample of 416 in utero exposed from the Stolin district in Brest, 85 percent of whom have been located. In my discussion with Dr Okeanov (see below) I was satisfied that we could put together a much larger sample of mothers of children born in the months after Chernobyl, a sample that could be collated with the measurement file. How many would have had measurements remains to be seen. Dr Voronetsky guessed that 5-7 percent of the WHO file from Mogilev and Gomel might have had measurements.

COMMUNICATION WITH THE BELAM STAFF During the first staff meeting I asked Dr Krisenko abut channels of communication between members of the US working group and the project staff. I told him we had been communicating directly but copying Dr Stozharov. He did not elaborate but merely said, in effect "Keep it up", by which I assume that we should copy Dr Rzheutski when writing to his staff. I doubt that Dr Krisenko will want to see cc of everything.

DR MINCEY I found Dr Mincey impressively knowledgeable and in excellent rapport with all but Dr Stozharov. He seems especially close to Mr Kuvshinnikov. He kindly took us to the opera twice (Carmen and Madame Butterfly) and to his comfortable rented apartment. He said he was on board until 19 December, after which his participation had not been arranged. This disturbed me and I took the matter up with Dr Wachholz who was reassuring after he had talked with Dr Mincey. Dr Mincey obviously knows well how to live off the local economy and introduced us to a couple of stores where he purchases food. He projected energy, great interest in the project, and influence on the staff. I can't imagine how we would do without him or some one like him, for long. Dr Polanskaya spoke well of him.

It was obvious that Dr Mincey was in need of a petty cash account. On at least two occasions he provided an interpreter, a professor in the language institute in Minsk.

PROTOCOL CHANGES We need to have the advisory group established soon as we are likely to face requests to change the protocol once the work gets started, especially in light of the difficulties we face in locating subjects and the possibility of using the Brest material. Dr Mincey mentioned a change in the Manual that might involve a change in the protocol but its precise nature does not appear in my notes. Dr Rzheutski was asking for changes in the consent form at one point, expressing concern that it did not

reflect the duration of the project or the fact that treatment would be provided if indicated. When I mentioned the bureaucratic complexity involved in changing the form he settled on the idea of mentioning treatment in the letter of invitation to be signed by the Minister (or Dr Krisenko?).

DR OKEANOV I made a courtesy call to Dr Okeanov whom I had been unable to visit in May. To my surprise, having been informed in 1991 that there were but 15 K clean-up workers in Belarus, he informed me that he had a study with the EC of 45 K clean-up workers with service in 1986-87. He is looking at all forms of cancer and believes he is finding excess leukemia, thyroid cancer, and cancer of urinary organs. He reported on this work in Geneva. The excess leukemia was seen in clean-up workers who had spent considerable time within the 30-km zone. I found the presentation in Geneva disappointing in that it lacked evidence of a critical examination of alternatives to the radiation etiology, and of diagnostic validity. Dr Cardis said she had felt it necessary to revise completely her joint EC paper with him.

Dr Okeanov is making quarterly reports on the Chernobyl and cancer registries. I asked that he put me on his mailing list and promised to send him copies of papers from NCI.

In discussing our in utero problem Dr Okeanov said there was a maternity hospital in each district and that we should have no trouble putting together a large sample of mothers of children born in the months after the accident, some of whom would have had direct thyroid measurements in 1986. Unfortunately I failed to ask how long the appropriate records were kept. At the oblast level there is no ID information, only numbers.

Dr Okeanov said he was still interested in working with Dr Tom Mason of the University of South Florida on mapping but had had no word of the fate of the Belarussian application to the US State Department for funding scientific projects. I promised to call Dr Mason and discuss the situation with him. Meanwhile he had obtained the software developed by the Sakarov Institute that Dr Robbins and I had seen in our visit to the Institute last May.

Dr Okeanov said he was the primary source of information on cancer, that Dr Averkin received copies from him. I explained that I had misunderstood this and in my meeting with Dr Averkin and Dr Korotkevich, Director of the Oncology Institute, I had assumed that the Oncology Institute was the primary source and, therefore, better equipped to join the set of cancer registries the NCI invited to participate in an occasional study. I apologized if it appeared that I had approached the wrong group. It may still be the case that the Oncology Institute has more direct access to the underlying medical record in the oncology dispensaries.

VISIT TO THE ONCOLOGY INSTITUTE I had also made a courtesy call at

the Oncology Institute, this time in the company of Dr Voronetsky. I had two purposes in mind: (1) to suggest to Dr Averkin that he publish information on the thyroid cancer incidence of children born after the accident; and (2) to explain the possibility of submitting a proposal to NCI to join the circle of cancer registries in the MAO/RFP program. I suggested that Dr Averkin might like to talk with Dr Timo Hakulinen of Finland and Dr Hans Storm of Denmark, both of whom are participants in the program. I promised to send some descriptive material. They showed no great interest in the idea but said they would be happy to review whatever I might send.

Dr Averkin indicated that the Institute had an agreement with Dr Abelin of Switzerland covering epidemiologic work on all forms of cancer, not just thyroid cancer. To date, however, only thyroid cancer had been the subject of collaboration.

HIGHLIGHTS OF THE VISIT TO MINSK

(1) Clarification of the responsibility for building the cohort
(2) Learning of the urgency for establishing the screening center in Gomel
(3) Putting the finishing touches on the case-control paper for the WHO meeting, and learning of the published case-control study in the RF by Ivanov, Tsyb, et al.
(4) Seeing the DCC set up and in operation and the preparations for a project office across the hall on the 6th floor
(5) Attending Dr Krisenko's brief staff meetings and learning of preparations for a pilot run of screening in December at the Minsk Dispensary
(6) Learning of the assigned roles of Drs Danilova and Drozd
(7) Improvements in the design of several critical study forms by Dr Robbins and Dr Danilova, and by Dr Brill and Dr Drozd
(8) The installation by Dr Brill and Mr Kuvshinnikov of special software (?and hardware) for managing the US data
(9) Discussion of the initial interview with an impressive professional from the Institute of Sociology of the Academy of Science
(10) Beginning the development of tasks and subtasks for contracts expected to provide local assistance to the personnel of he project
(11) Learning of the attitudes of Drs Stozharov and Voronetsky toward the use of the Brest measurement in the BelAm project
(12) Seeing Dr Mincey in operation
(13) Understanding the need for the early appointment of the Oversight Group

Attachments (8)

CIT 1.a

16 November, 1995

Memorandum for Dr Krisenko

Subject: Selection of BelAm Cohort

The present situation is critical because:

(1) Only 600 potential cohort subjects have been pulled from the measurement file, and only half of these have current addresses. In addition, it appears that nearly all of these 600 live far away from the Minsk dispensary(Gomel Oblast).

(2) Creation of a significant number of potential cohort subjects, say, 2,000-3,000, with which to start the main screening effort, will take time.

(3) We are on the verge of a pilot run in the dispensary that will create a momentum looking toward initiation of the regular screening operation that we hope will be continuous, once started.

(4) There was uncertainty here as to the responsibility for the first step to create the cohort, i.e., to mobilize the information in the measurement file needed to begin locating potential subjects for the cohort. Dr Stozharov seemed to be in a position to facilitate the decision as to responsibility, and agreed to call a meeting of the Moscow and Minsk groups to settle the matter. Later, I learned from Dr Bouville that he believed all the information in Moscow had been placed on diskette and provided to both the Minsk dosimettry group and the DCC. If this is correct, it means that we are ready to start now, in the Epidemiology group and the DCC, to establlish current addresses in order to begin screening.

(5) The measurement file of about 39,000 (not 28,000) good measurements on children under 18 in 1986 seems now to be available for the address search and for updating with new address information and with other available information that will be useful to the project (parental names, identifying numbers, existing thyroid diagnoses, etc). The responsible groups here will, however, need your influence in order to obtain access to medical and other files that are expected to contain current address information. Only some of these will be computer files. The project may also want to call on other organizations for services in matching their files to the BelAm cohort, and requests for such assistance might well require your authority. An example would be the files of the

Ministry of Internal Affairs.

(6) On the basis of discussions today, I believe a concrete plan to obtain the addresses needed for the cohort will be prepared soon by Dr Voronetsky and Mr Kuvshinnikov. Dr Voronetsky has essentially completed a preliminary survey of 600 representative names drawn from the measurement file a year or more ago, and his experience can be used in planning an efficient strategy to obtain addresses from the file of 39,000.

Incidentally, Mr Kuvshinnikov finds that the measurement file of 39,000 here breaks down into approximately : 22,000 under 0.3 Gy, 11,000 between 0.3 and 1 Gy, and 6,000 over 1 Gy.

Thank you for your attention to this matter.

Gilbert W. Beebe PhD

DISPENSARY	86	600
WHO	20	600
REGIONS	137	525
LETTERS	23	40
OKEANOV	149	600
PHONES DB	19	28

	WHO	DISPENSARY	REGIONS	OKEANOV	PHONES DB	LETTERS
WHO	20	1	0	15	0	0
DISPENSARY	1	86	1	36	0	2
REGIONS	0	1	137	41	0	0
OKEANOV	15	36	41	149	0	2
PHONES DB	0	0	0	0	19	0
LETTERS	0	2	0	2	0	23

Tables from Dr Voronetsky, 25 May, 1995, summarizing the experience in identifying and locating the sample of 600 taken from the "measurement file"

3a

DRAFT

August 19, 1995

SCIENTIFIC PROTOCOL FOR THE STUDY OF THYROID CANCER AND OTHER THYROID DISEASE IN BELARUS FOLLOWING THE CHERNOBYL ACCIDENT

PROPOSAL TO MODIFY SAMPLING PLAN

Introduction As operational planning began it became known that the measurement file on which the sampling plan was based (section 3.2) lacked specific addresses and, in many instances, complete names and birth dates. It seemed essential, therefore, that an exploratory effort be made to examine the feasibility of locating individuals in the measurement file. A representative sample of 600 names was drawn from the file for those 0-18 at the time of the accident, and a determined effort made to locate them. The result of that effort, briefly described below, indicated that, starting with names in the measurement file, it would be difficult to locate more than about 70 percent of the potential subjects. While the pilot was in progress, it was learned that there was a second measurement file of about 25,000 children whose measurements had been made in the Brest oblast, and that many of the measurements were consistent with thyroid doses of one Gy or more.

Since the sampling plan of the protocol made use of different sampling ratios for those with presumptive doses of 0-.29, 0.3-.99, and 1 or more Gy, 200 names were selected at random within each of these dose groups for a total of 600. These names were then taken to a variety of file sources for identification and address information (table 1). (We need here a brief description of the individual sources listed in the table). The table shows not only the number found in each file, but also the relationship of one file to another. For example, of the 137 identified in oblast files, 42 were also found in the other files, principally the central Chernobyl Registry. Of the 149 found in the Chernobyl Registry, 93 were found in other files.

A study cohort representing only 70 percent of the 1986 measurement file would not permit strong statements to be made about its thyroid experience in the interval 1986-1996 or whenever the clinical examinations begin. A possible alternative to taking the measurement file to each manual file in a record room is, of course, to start with the source file and map it into

the measurement file. In some instances this may be the easier pattern of file-searching. Whether one maps the measurement file into the source file or vice versa, of course, does not affect the ultimate matching rate, the expected 70 percent, or confer any advantage as to the credibility of inferences that may be drawn about risk in the pre-project period. If the source file is automated, of course, as are the Chernobyl Registry and a few other files, direct computer matching is in order.

The Brest files have been under investigation in the Institute of Radiation Medicine and the Institute of Biophysics in Moscow. The preliminary indications are that some of this file, at least, may be useful and thus provide a larger pool of high-dose subjects to choose from.

PROPOSAL In view of the possibility that not all the hoped-for 5,000 subjects with doses of 1 Gy or more can be located, it is proposed that the sampling criteria be changed to accept into the cohort all available children with doses over 0.5 Gy. The objective of 4,000 with doses under 0.3 Gy would be retained, and the balance of the 15,000 would be the 0.3-.49 category.

It is further proposed that the Brest file, or whatever portion of it proves acceptable to the dosimetrists n Moscow and Kiev, be given the same status as the Moscow measurement file, with full use of those with presumptive doses of 0.5 or more Gy, and proportionate use of those in the two lower dose intervals.

If accepted, the two foregoing proposals would materially change the research protocol approved in May, 1994.

In addition to the source files used for the pilot investigation of the 600 names on the Moscow measurement file, it is proposed that negotiations be entered into with the Ministry of Internal affairs to identify and locate older members of the two measurement files, those that would have attained age 18 or older since the Chernobyl accident and, therefore, have received passport numbers.

Whether each manual source file is mapped into the measurement file, or vice versa, it should be possible to retain a record of all the files in which the subject was found and, more important, to capture the earliest date on which the subjec came under observation by that source. e.g., as an

addition to the Chernobyl Registry. This information may be useful in studying the pre-project period, 1986-1996.

3c

IMPLICATIONS AND UNRESOLVED ISSUES The potential availability of the Brest file makes it possible to re-consider the sample-size restraint imposed by the protocol adopted in 1994, 15,000. If it should be shown that a sample size greater than 15,000, with greater power to detect cancer and other thyroid disease, could be assembled, then it would be possible to re-open the question of total sample size. At this time, however, the question should be held in abeyance as being hypothetical.

As noted above, the pilot work on the sample of 600 indicates that we can expect only about 70 percent to be available. This estimate may change if the passport files of the Ministry of Chernobyl should become accessible and prove fruitful, and if it proves very much easier to locate subjects on the Brest file of measurements than those on the Moscow file. But it is unlikely that the identification and address location of subjects in these files will approach the point at which we can feel confident of having unbiased estimates of risk in the pre-project period. We can expect to have unbiased estimates of risk in the prospective period initiated by the beginning of the project, however.

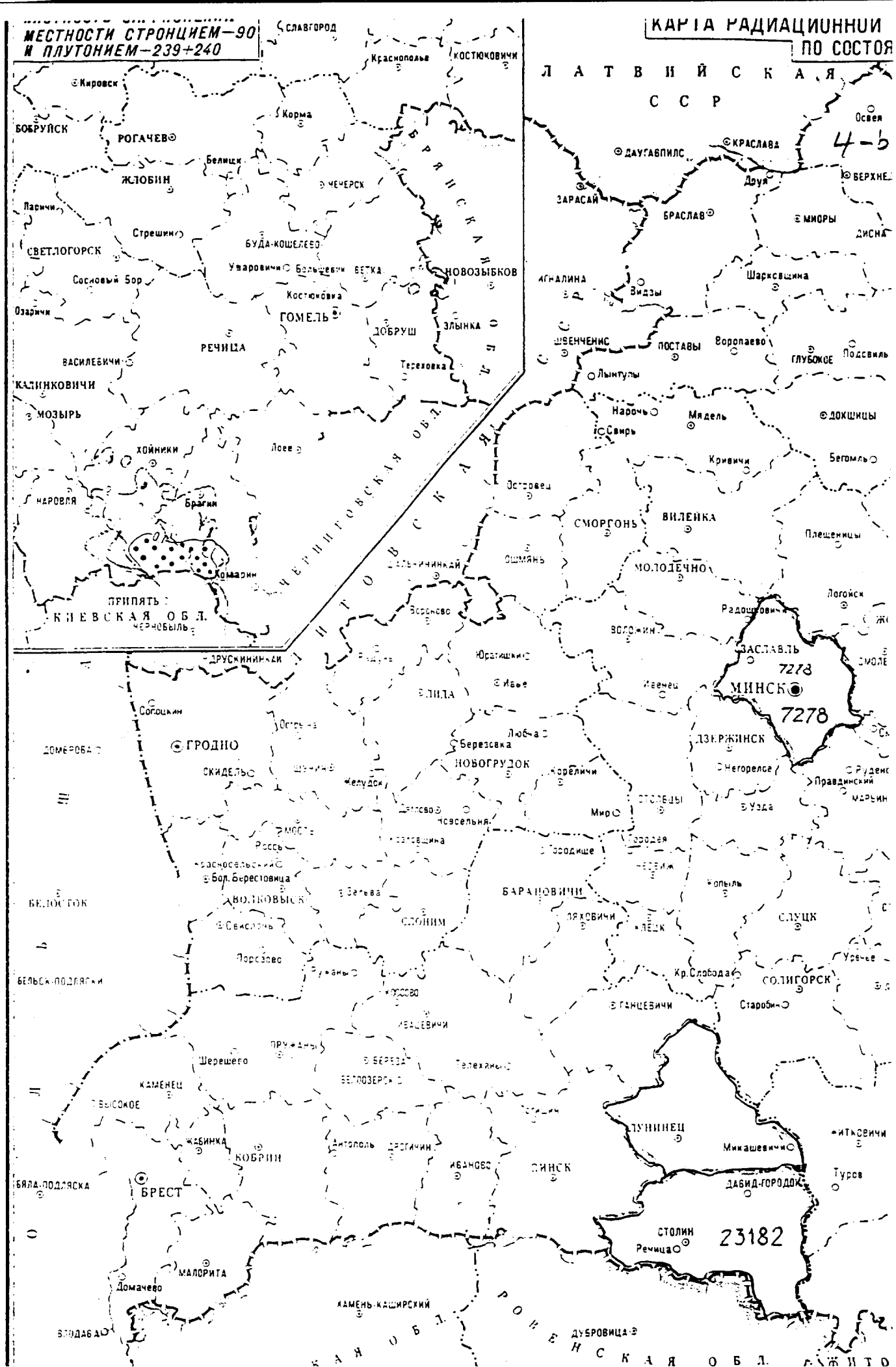
Table 1 Results of Searching 600 Sample Names in Various Source Files

Source Letters	WHO	Dispensary	Source Regions	Okeanov	Phones DB
WHO	20	1		15	
Dispensary	1	86	1	36	
2 Regions		1	137	41	

3d.

Okeanov	15	36	41	**149**	
2					**19**
Phones DB		2		2	
Letters					
23					

Note: Numbers printed in **bold** type are the total number of subjects located by each source among the 600 except that 525 were sent to the "regions", only 40 letters were written, and 28 were sought via "phones DB".


МЕСТНОСТИ СТРОНЦИЕМ-90
И ПЛУТОНИЕМ-239+240
КАРТА РАДИАЦИОННОЙ
ПО СОСТОЯ
4-b
ЛАТВИЙСКАЯ
ССР
СЛАВГОРОД
Краснополье
КОСТЮКОВИЧИ
Кировск
БОБРУЙСК
РОГАЧЕВ
Корма
Белицк
ЖЛОБИН
ЧЕЧЕРСК
БРЯНСКАЯ
Лавичи
Стрешин
СВЕТЛОГОРСК
БУДА-КОШЕЛЕВО
Уваровичи
Большевик
БЕТКА
НОВОЗЫБКОВ
Сосновый Бор
Костюковка
Озаричи
ГОМЕЛЬ
ДОБРУШ
ЗЛЫНКА
РЕЧИЦА
Тереховка
ВАСИЛЕВИЧИ
КАЛИНКОВИЧИ
МОЗЫРЬ
ЧЕРНИГОВСКАЯ ОБЛ.
Лоев
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НАРОВЛЯ
Брагин
Комарин
ПРИПЯТЬ
КИЕВСКАЯ ОБЛ.
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КРАСЛАВА
Освея
Даугавпилс
Дуя
ЗАРАСАЙ
БРАСЛАВ
МИОРЫ
ДИСНА
АГАЛИНА
Видзы
Шарковщина
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ПОСТАВЫ
Воропаево
ГЛУБОКОЕ
Подсвиль
Лынтупы
Нарочь
Мядель
ДОКШИЦЫ
Свирь
Кривичи
Островец
СМОРГОНЬ
ВИЛЕЙКА
Плещеницы
ОШМЯНЬ
МОЛОДЕЧНО
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Радошковичи
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ДРУСКИНИНКАЙ
Юратишки
ЛИДА
Ивье
Ивенец
Сопоцкин
ГРОДНО
Любча
Березовка
ДЗЕРЖИНСК
ДОМЕРОВА
СКИДЕЛЬ
НОВОГРУДОК
Кореличи
Негорелое
Правдинский
Желудок
Мир
Узда
Рось
Городея
Городище
Красносельский
Бол. Берестовица
Зельва
БАРАНОВИЧИ
Копыль
БЕЛОСТОК
ВОЛКОВЫСК
Свислочь
СЛОНИМ
ЛЯХОВИЧИ
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Порозово
Кр. Слобода
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Старобин
Ивацевичи
Шерешево
Пружаны
БЕРЕЗА
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Житковичи
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РОВЕНСКАЯ ОБЛ.

Й ОБСТАНОВКИ НА ТЕРРИТОРИИ БССР
ОЯНИЮ НА ЯНВАРЬ 1990 г.

Source of Measurement A6
Where mes are made in 1986

4a

ПЛОТНОСТЬ ЗАГРЯЗНЕНИЯ МЕСТНОСТИ ЦЕЗИЕМ–137

УСЛОВНЫЕ ОБОЗНАЧЕНИЯ

ПО ЦЕЗИЮ-137

- изолинии загрязнения 1 Ku/кв. км
- изолинии загрязнения 5 Ku/кв. км
- изолинии загрязнения 15 Ku/кв. км
- изолинии загрязнения 40 Ku/кв. км
- зона загрязнения от 1 до 5 Ku/кв. км
- зона загрязнения от 5 до 15 Ku/кв. км
- зона загрязнения от 15 до 40 Ku/кв. км
- зона загрязнения свыше 40 Ku/кв. км

ПО СТРОНЦИЮ-90

- изолинии загрязнения 1 Ku/кв. км
- изолинии загрязнения 2 Ku/кв. км
- изолинии загрязнения 3 Ku/кв. км
- зона загрязнения от 1 до 2 Ku/кв. км
- зона загрязнения от 2 до 3 Ku/кв. км
- зона загрязнения свыше 3 Ku/кв. км

ПО ПЛУТОНИЮ-239 +240

- 0.1 изолинии загрязнения 0.1 Ku/кв. км
- зона загрязнения свыше 0.1 Ku/кв. км

Масштаб 1:2 000 000
в 1 сантиметре 20 километров

УСЛОВНЫЕ ОБОЗНАЧЕНИЯ

НАСЕЛЕННЫЕ ПУНКТЫ

- МИНСК — столицы союзных республик
- ВИТЕБСК — центры областей
- МОЗЫРЬ ЕЛЬСК Лоев — центры районов
- ЗАСЛАВЛЬ Мир — прочие города и поселки городского типа, ВАСИЛЕВИЧИ

ГРАНИЦЫ

- государств
- областей
- районов

Составлено с использованием радиационных обследований выполнено Белорусским управлением по гидрометеорологии
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Управление геодезии и картографии при Совете Министров СССР
Москва 1990

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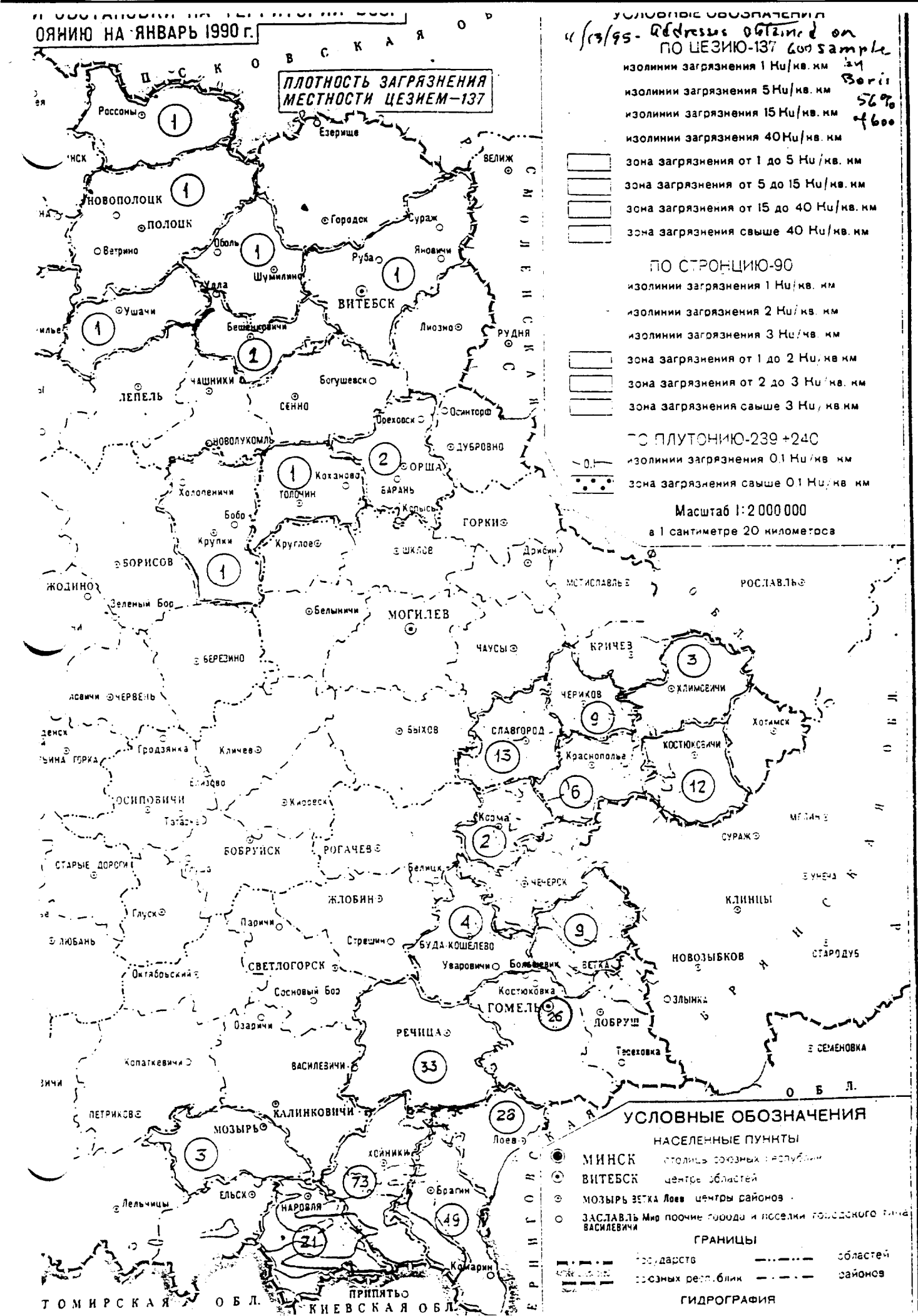

Составление элементов радиационной обстановки выполнено Белорусским управлением по гидрометеорологии.
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Москва 1990

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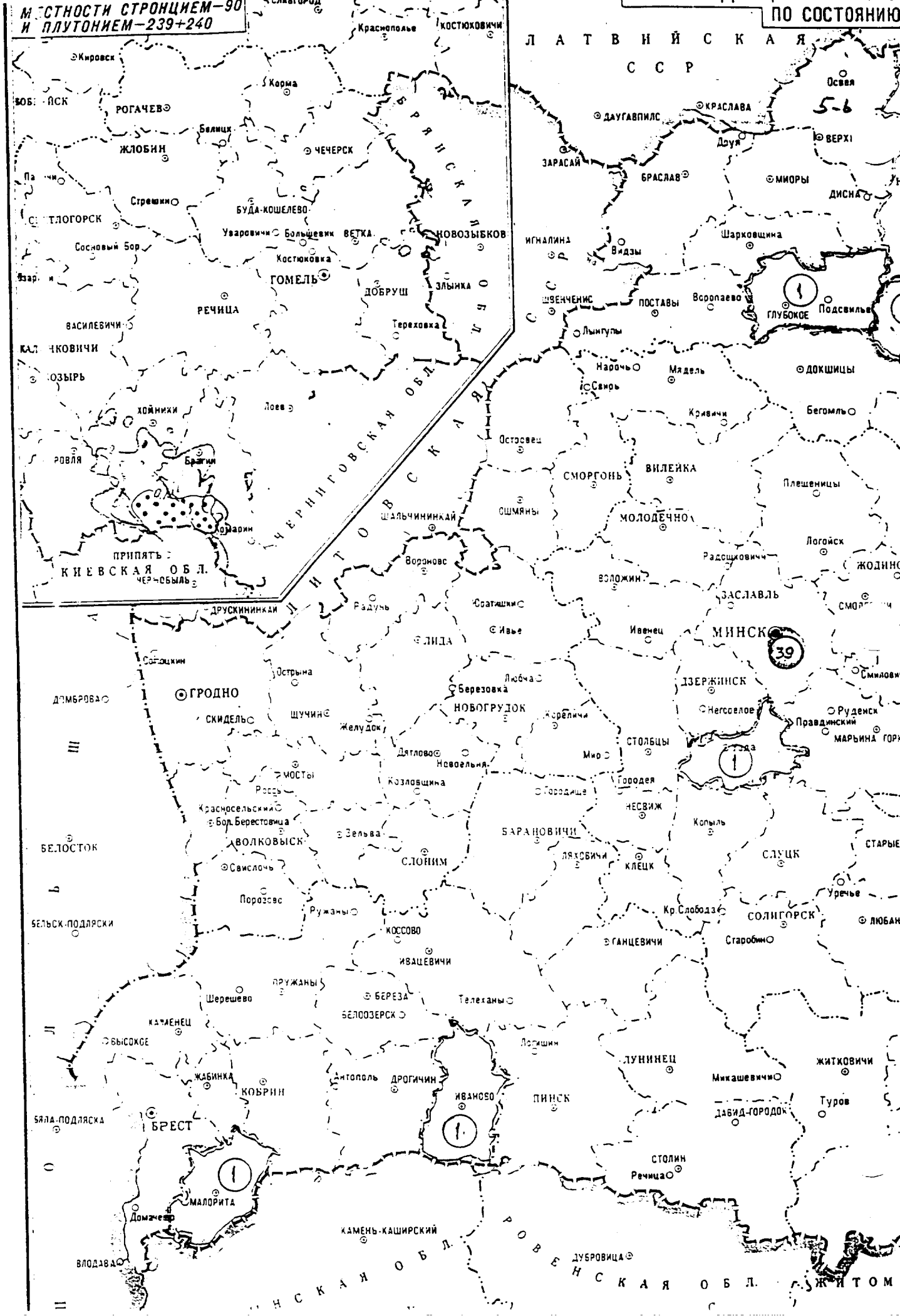
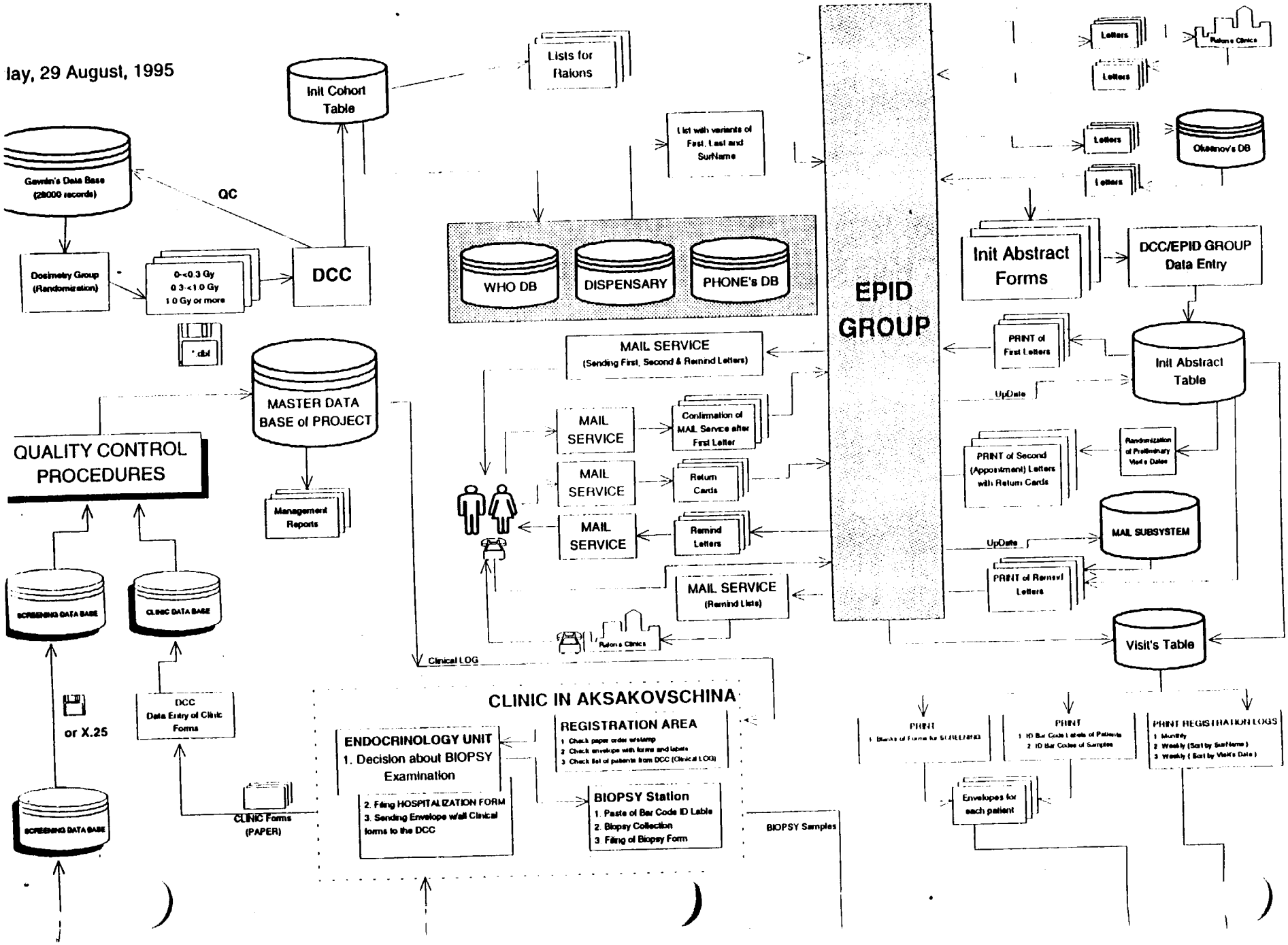


МЕСТНОСТИ СТРОНЦИЕМ-90
И ПЛУТОНИЕМ-239+240

ПО СОСТОЯНИЮ

5-6

lay, 29 August, 1995



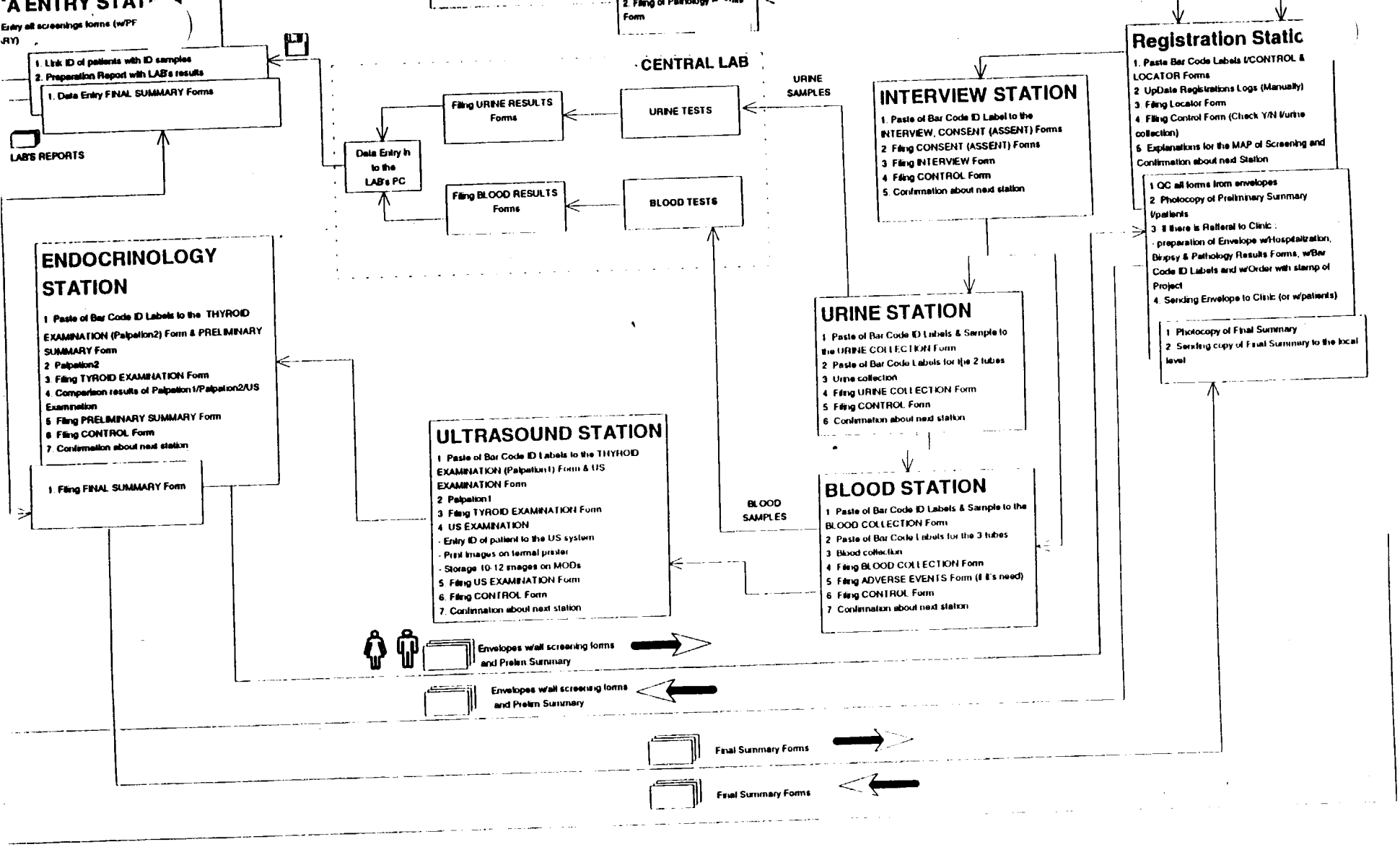

A ENTRY STAT
Entry all screenings forms (w/PF
RY)
1. Link ID of patients with ID samples
2. Preparation Report with LAB's results
1. Data Entry FINAL SUMMARY Forms
LAB'S REPORTS
2. Filing of Pathology
Form
CENTRAL LAB
Filing URINE RESULTS Forms
URINE TESTS
Data Entry In to the LAB's PC
Filing BLOOD RESULTS Forms
BLOOD TESTS
URINE SAMPLES
INTERVIEW STATION
1. Paste of Bar Code ID Label to the INTERVIEW, CONSENT (ASSENT) Forms
2. Filing CONSENT (ASSENT) Forms
3. Filing INTERVIEW Form
4. Filing CONTROL Form
5. Confirmation about next station
Registration Static
1. Paste Bar Code Labels I/CONTROL & LOCATOR Forms
2. UpDate Registrations Logs (Manually)
3. Filing Locator Form
4. Filing Control Form (Check Y/N I/urine collection)
5. Explanations for the MAP of Screening and Confirmation about next Station
1. QC all forms from envelopes
2. Photocopy of Preliminary Summary I/patients
3. If there is Referral to Clinic :
- preparation of Envelope w/Hospitalization, Biopsy & Pathology Results Forms, w/Bar Code ID Labels and w/Order with stamp of Project
4. Sending Envelope to Clinic (or w/patients)
1. Photocopy of Final Summary
2. Sending copy of Final Summary to the local level
ENDOCRINOLOGY STATION
1. Paste of Bar Code ID Labels to the THYROID EXAMINATION (Palpation2) Form & PRELIMINARY SUMMARY Form
2. Palpation2
3. Filing TYROID EXAMINATION Form
4. Comparison results of Palpation1/Palpation2/US Examination
5. Filing PRELIMINARY SUMMARY Form
6. Filing CONTROL Form
7. Confirmation about next station
1. Filing FINAL SUMMARY Form
URINE STATION
1. Paste of Bar Code ID Labels & Sample to the URINE COLLECTION Form
2. Paste of Bar Code Labels for the 2 tubes
3. Urine collection
4. Filing URINE COLLECTION Form
5. Filing CONTROL Form
6. Confirmation about next station
ULTRASOUND STATION
1. Paste of Bar Code ID Labels to the THYROID EXAMINATION (Palpation1) Form & US EXAMINATION Form
2. Palpation1
3. Filing TYROID EXAMINATION Form
4. US EXAMINATION
- Entry ID of patient to the US system
- Print images on termal printer
- Storage 10-12 images on MODs
5. Filing US EXAMINATION Form
6. Filing CONTROL Form
7. Confirmation about next station
BLOOD SAMPLES
BLOOD STATION
1. Paste of Bar Code ID Labels & Sample to the BLOOD COLLECTION Form
2. Paste of Bar Code Labels for the 3 tubes
3. Blood collection
4. Filing BLOOD COLLECTION Form
5. Filing ADVERSE EVENTS Form (if it's need)
6. Filing CONTROL Form
7. Confirmation about next station
Envelopes w/all screening forms and Prelim Summary
Envelopes w/all screening forms and Prelim Summary
Final Summary Forms
Final Summary Forms

Fig 9

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АДМИНИСТРАТИВНАЯ ГРУППА (Н.А. КРЫСЕНКО)
? ЧЕЛ.

ГРУППА ЭПИДЕМИОЛОГИИ	ЦЕНТР КООРДИНАЦИИ ДАННЫХ	ГРУППА ДОЗИМЕТРИИ	КЛИНИЧЕСКАЯ ГРУППА	СКРИНИНГОВЫЙ ЦЕНТР	ЦЕНТРАЛЬНАЯ ЛАБОРАТОРИЯ	ГРУППА КОНТРОЛЯ КАЧЕСТВА
Б.К.ВОРОНЕЦКИЙ	А.В.КУВШИННИКОВ	В.Ф.МИНЕНКО	Л.И.ДАНИЛОВА	В.А.РЖЕУТСКИЙ	С.В.ПЕТРЕНКО	М.М.ОРЛОВ
6 ЧЕЛ.	7 ЧЕЛ.	5 ЧЕЛ.	4 ЧЕЛ.	9 ЧЕЛ.	3 ЧЕЛ.	3 ЧЕЛ.
Voronetsky	Kuvshinnikov	Minenko	Danilova	Rzeutski	Petrenko	Orlov

11/23/95 for Kir
S.a

Notes on Tasks and Sub-tasks

1) Management/Administration
   - Project Director, plus staff
   - Interpreter, exec secy, driver, Administrator
   - Subtasks:
     - To administer the project
     - Travel, meetings, etc
     - Personnel management
     - Supply and equipment
     - Space and communication
     - Transportation
     - Reporting to Ministry, to Advisory Group
     - Contractual obligations
     - Quality control
     - Arrange tests of various screening modules, etc
     - Arrange start of first formal screening cycle
     - Establish reporting system for operations of all kinds

2) Establish the Cohort as Defined in Protocol
   - Prepare a single file of the measurements made in 1986
     - Uniform format
     - Containing all available information useful in locating the subject
     - Delete any with measurements considered useless, duplicates, etc
   - Acquire access to machinable files for record linkage
   - Develop matching criteria for each such machinable file
   - Match each such file to the single file of measurements (the "file")
     - Update the file with result of match
     - Copy from borrowed file any information needed to locate subject or any essential medical information (define "essential information")
     - Copy good matches for the "cohort"
   - Acquire access to potentially useful non-machinable files
   - Estimate usefulness of each by testing small representative sample
   - Develop matching procedures
   - Perform the match and repeat operations as above
   - Plan and carry out other types of address searches not covered by file searches