MATERIALS LICENSE

Pursuant to the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974 (Public Law 93-438), and Title 10, Code of Federal Regulations, Chapter I, Parts 30, 31, 32, 33, 34, 35, 36, 39, 40, and 70, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, possess, and transfer byproduct, source, and special nuclear material designated below; to use such material for the purpose(s) and at the place(s) designated below; to deliver or transfer such material to persons authorized to receive it in accordance with the regulations of the applicable Part(s). This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, as amended, and is subject to all applicable rules, regulations, and orders of the Nuclear Regulatory Commission now or hereafter in effect and to any conditions specified below.

Licensee	
1. AttoChrom/Bio Traces, Inc.	3. License Number 37-30283-01
2. Ben Franklin Technology Center 115 Research Drive, Suite 136 Bethlehem, Pennsylvania 18015	4. Expiration Date August 31, 2001
	5. Docket or Reference No. 030-34088

6. Byproduct, Source, and/or Special Nuclear Material	7. Chemical and/or Physical Form	8. Maximum Amount that Licensee May Possess at Any One Time Under This License
A. Iodine 125	A. Any	A. 5 millicuries

9. Authorized use

A. Research and development as defined in 10 CFR 30.4.

CONDITIONS

10. A. Licensed material may be used only at the licensee's facilities located at Room 136 of Jordan Hall, 115 Research Drive, Bethlehem, Pennsylvania, and Room C-260 of Iacocca Hall, 111 Research Drive, Bethlehem, Pennsylvania.

B. The licensee may not possess and use materials authorized in Items 6, 7, and 8, until: (1) the licensee has constructed the facilities and obtained the equipment described in the application and supporting documentation; and (2) the U.S. Nuclear Regulatory Commission, Region I, ATTN: Chief, Nuclear Materials Safety Branch, 475 Allendale Road, King of Prussia, Pennsylvania 19406 has been notified in writing that activities authorized by the license will be initiated.

In accordance with the requirements set forth in 10 CFR 30.36(b), 40.42(b), and 70.38(b), the licensee shall promptly notify the Nuclear Regulatory Commission, in writing, of a decision not to complete the facility, acquire equipment, or possess and use authorized material.

11. A. Licensed material shall be used by, or under the supervision of Roman Bielski, Ph.D.

B. The Radiation Safety Officer for this license is Roman Bielski, Ph.D.

12. Licensed material shall not be used in or on human beings.

13. The licensee shall not use licensed material in field applications where activity is released except as provided otherwise by specific condition of this license.

MATERIALS LICENSE
SUPPLEMENTARY SHEET

License Number: 37-30283-01
Docket or Reference Number: 030-34088

14. The licensee is authorized to hold radioactive material with a physical half-life of less than or equal to 120 days for decay-in-storage before disposal in ordinary trash, provided:

    A. Waste to be disposed of in this manner shall be held for decay a minimum of ten half-lives.

    B. Before disposal as ordinary trash, the waste shall be surveyed at the container surface with the appropriate survey instrument set on its most sensitive scale and with no interposed shielding to determine that its radioactivity cannot be distinguished from background. All radiation labels shall be removed or obliterated.

    C. A record of each such disposal permitted under this License Condition shall be retained for three years. The record must include the date of disposal, the date on which the byproduct material was placed in storage, the radionuclides disposed, the survey instrument used, the background dose rate, the dose rate measured at the surface of each waste container, and the name of the individual who performed the disposal.

15. The licensee is authorized to transport licensed material in accordance with the provisions of 10 CFR Part 71, "Packaging and Transportation of Radioactive Material."

16. Except as specifically provided otherwise in this license, the licensee shall conduct its program in accordance with the statements, representations, and procedures contained in the documents, including any enclosures, listed below. The Nuclear Regulatory Commission's regulations shall govern unless the statements, representations, and procedures in the licensee's application and correspondence are more restrictive than the regulations.

    A. Application dated February 9, 1996
    B. Letter dated June 17, 1996
    C. Letter dated August 4, 1996

For the U.S. Nuclear Regulatory Commission

Original Signed By:
Elizabeth Ullrich

Date SEP - 4 1996

By _____

Division of Nuclear Materials Safety
Region I
King of Prussia, Pennsylvania 19406

SEP - 4 1996

License No. 37-30283-01
Docket No. 030-34088
Control No. 122952

Roman Bielski, Ph.D.
Radiation Safety Officer
AttoChrom/BioTraces, Inc.
Ben Franklin Technology Center
115 Research Drive, Suite 136
Bethlehem, PA 18015

Dear Dr. Bielski:

Please review the enclosed document carefully and be sure that you understand all conditions. If there are any errors or questions, please notify the U.S. Nuclear Regulatory Commission, Region I Office, Licensing Assistance Team, (610) 337-5093 or 5239, so that we can provide appropriate corrections and answers.

Please be advised that your license expires at the end of the day, in the month, and year stated in the license. Until your license is terminated, you must conduct your program involving byproduct materials in accordance with the conditions of your NRC license, representations made in your license application, and NRC regulations. In particular, note that you must:

1. Operate in accordance with NRC regulations 10 CFR Part 19, "Notices, Instructions and Reports to Workers; Inspections," 10 CFR Part 20, "Standards for Protection Against Radiation," and other applicable regulations.

2. Not possess and use materials authorized in Items 6, 7, and 8, on the license until:

   a. you have constructed the facilities and obtained the equipment described in the license application and supporting documentation; and

   b. you have notified the U.S. Nuclear Regulatory Commission, Region I, ATTN: Chief, Nuclear Materials Safety Branch, 475 Allendale Road, King of Prussia, Pennsylvania 19406 in writing, that activities authorized by the license will be initiated.

3. Notify NRC, in writing, within 30 days:

   a. when an authorized user or Radiation Safety Officer, permanently discontinues performance of duties under the license or has a name change; or

b. when the mailing address on the license changes (no fee is required if the location of byproduct material remains the same).

4. In accordance with 10 CFR 30.36(b) and/or license condition, notify NRC, promptly, in writing, and request termination of the license:

   a. when you decide to terminate all activities involving materials authorized under the license; or

   b. if you decide not to complete the facility, acquire equipment, or possess and use authorized material.

5. Request and obtain a license amendment before you:

   a. permit anyone to work as an authorized user under the license;

   b. change Radiation Safety Officer;

   c. order byproduct material in excess of the amount, or radionuclide, or form different than authorized on the license;

   d. add or change the areas of use, or address or addresses of use identified in the license application or on the license; or

   e. change ownership of your organization.

6. Submit a complete renewal application with proper fee or termination request at least 30 days before the expiration date of your license. You will receive a reminder notice approximately 90 days before the expiration date. Possession of byproduct material after your license expires is a violation of NRC regulations. A license will not normally be renewed, except on a case-by-case basis, in instances where licensed material has never been possessed or used.

In addition, please note that NRC Form 313 requires the applicant, by his/her signature, to verify that the applicant understands that all statements contained in the application are true and correct to the best of the applicant's knowledge. The signatory for the application should be the licensee or a certifying official of the licensee rather than the Radiation Safety Officer or a consultant.

You will be periodically inspected by the NRC. Failure to conduct your program in accordance with NRC regulations, license conditions, and representations made in your license application and supplemental correspondence with NRC will result in enforcement action against you. This could include issuance of a notice of violation, or imposition of a civil penalty, or an order suspending, modifying or revoking your license as specified in the "General Statement of Policy and Procedure for NRC Enforcement Actions," (Enforcement Policy), NUREG 1600.

Since serious consequences to employees and the public can result from failure to comply with NRC requirements, prompt and vigorous enforcement action will

be taken when dealing with licensees who do not achieve the necessary meticulous attention to detail and the high standard of compliance which NRC expects of its licensees.

Thank you for your cooperation.

Sincerely,

ORIGINAL SIGNED BY:

Elizabeth Ullrich
Senior Health Physicist
Nuclear Materials Safety Branch 2
Division of Nuclear Materials Safety

License No. 37-30283-01
Docket No. 030-34088
Control No. 122952

Enclosures:
1. License No. 37-30283-01
2. 10 CFR Parts 2, 19, 20, 30, and 170
3. NRC Forms 3 and 313

cc:
E. James Wadiak, President
BioTraces, Inc.
10517-A West Drive
Fairfax, VA 22030

DOCUMENT NAME: R:\WPS\MLTR\L3730283.01
To receive a copy of this document, indicate in the box: "C" = Copy w/o attach/encl "E" = Copy w/ attach/encl "N" = No copy

OFFICE	DNMS/RI	N	DNMS/RI					
NAME	SLodhi		EUllrich					
DATE	08/20/96		08/ /96		08/ /96		08/ /96	

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ATTOCHROM

Division of BioTraces, Inc.

115 Research Drive
Bethlehem, PA 18015-4734

tel: (610) 861-6948
fax: (610) 861-8247

Roman Bielski, Ph.D.

Bethlehem, 08/04/96

Dr. Elizabeth Ullrich, Senior Health Physicist,
Nuclear Materials Safety Branch 2,
Division of Nuclear Materials Safety,
United States Nuclear Regulatory Commission,
Region I,
475 Allendale Road,
King of Prussia, PA 19406-1415

Re: Application to US Nuclear Regulatory Commission, Mail control Number 122952.

Dear Dr Ullrich:

This letter is in reference to the telephone call from Dr. Sattar Lodhi on 07/30/96. I will try to resolve all the issues Dr. Lodhi raised regarding my 06/17/96 letter in his kind call. My answers or modifications made because of the issues raised are itemized below according to the 06/17/96 letter:

5. The room C-260 in the Iacocca Hall has a door with a combination lock. The combination is known to the users of the room but not to students and staff of the Lehigh University. This room consists of three parts: cold room, phosphorus and similar radioisotopes room and radio iodination room. The radio iodination room has a separate door. This room can be entered only from the inside of the room C-260. The door to the radio iodination room requires a normal key. Only few people from Lehigh University and Dr. Bielski have keys to this room. At this point nobody from LU is involved and plans to be involved in radio iodinations so we are the only party to use the room in the near future.

7. As it was already mentioned, we do not anticipate LU faculty or staff to use radio iodination room in the near future. Nevertheless, we will keep our radioactive samples not only in this room but in the safe box. This box will always stay in the fume hood in the radio iodination room.

The fume hood in room 136, Jordan Hall, which was recently installed, is connected to the outside of the building.

14. We did not, do not and will not send any radioactive compounds to ICN and similar companies. We will send non-radioactive compounds for radio iodinations and we expect such service company to use their own radioactive compounds or elements.

16. The instruction will include:

During iodinations or any other work with iodine-125 in the fume hood of the room C-260, Iacocca Hall, the Johnson GSM-115 meter must be present and switched on.

21. Landauer Inc. is the company we will purchase TLD badges from and the same company will be sent badges for measurements.

Yours sincerely

Roman Bielski

MNSB TELEPHONE CONVERSATION RECORD

Person Called: Dr. Roman Bielski, RSO — **Phone No.:** (610) 861 6948

Person Calling: Sattar Lodhi — **Date:** July 30, 1996

Facility Name: Attochrome/Biotraces, Inc. — **Time:** 9:30 a.m.

License No. New License Application (Mail Control 122952) **Docket No.** 030-34088

Subject: Elaboration of Response

Summary: I called Dr. Bielski to request some elaboration of his response to the deficiency letter. I requested him to address the following:

1. how the arrange with Lehigh University will ensure that the material will be secure at the facility;
2. arrangement to ensure radiation safety if there is a concurrent use of iodination facilities by Lehigh and Attochrome;
3. Is the hood in Rm 136 vented to the outside?
4. Will there be a transfer of I-125 to ICN Biologicals?
5. Laboratory instructions to include the necessity of security of licensed materials
6. Who will process the TLDs? (He already stated that Landauer will be the supplier as well as the processor)

Dr. Bielski will respond in about a week.

Action Required/Taken: Wait for his response

Signature: Sattar Lodhi — Mail Control No. 122952

BioTraces Inc.
10517-A West Drive
Fairfax, VA 22030

Office: tel: (703) 273-6941
fax: (703) 273-6968

June 18, 1996

Dr. Elizabeth Ulrich, Senior Health Physicist
Nuclear Materials Safety Branch 2
Division of Nuclear Materials Safety
United States Nuclear Regulatory Commission
Region 1
475 Allendale Road
King of Prussia, PA 19406-1415

RE: Application to US Nuclear Regulatory Commission, Mail Control Number 122952

Dear Dr. Ulrich:

This letter is in response to question #29 of your deficiency letter dated May 10, 1996 to Dr. Roman Bielski at the AttoChrom division of BIOTRACES, INC.

I hereby affirm that I have reviewed the original application for NRC license prepared by Dr. Roman Bielski as well as his follow-up letter responding to your deficiency letter dated May 10, 1996 and I concur with all the statements and representations contained therein.

If you have any further questions concerning management representations, you may call me directly at (703) 273-6941.

Sincerely,

E. James Wadiak
President

MS-16
Q2

ATTOCHROM *Division of BioTraces*
BFTC 115 Research Drive, Bethlehem, PA 18015 (610) 861-6948 (610) 861-8247 (Fax)

Roman Bielski, Ph.D. Bethlehem, 06.17.96

Dr. Elizabeth Ullrich, Senior Health Physicist,
Nuclear Materials Safety Branch 2,
Division of Nuclear Materials Safety,
United States Nuclear Regulatory Commission,
Region I,
475 Allendale Road,
King of Prussia, PA 19406-1415

Re: Application to US Nuclear Regulatory Commission, Mail Control Number 122952

Dear Dr. Ullrich:

Thank you for your letter of 05.10.96. We provide below our responses to the issues you raise in your letter. The answers refer to the numbers assigned to questions formulated in your letter.

1. Currently, the only person who will use and be responsible for the use of radioactive material (iodine 125) will be Dr. Roman Bielski. His formal training took place in Poland during his Masters studies at the Department of Chemical Technology, Warsaw Institute of Technology and Ph.D. studies at the Polish Academy of Sciences, Institute of Organic Chemistry. Details of Dr. Bielski's radiation training follows:

Type of Training	Location and Date(s) of Training	Duration of Training (in clock hours)		
		Formal Training	On the Job Training	Experience
Principles and practices of radiation protection	Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland; 1974 AttoChrom/BioTraces; 1994-96	12	20	 250
Radioactivity measurements standardization and monitoring techniques and instruments	Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland; 1974 AttoChrom/BioTraces; 1994-96	10	50	 180
Mathematics and calculations basic to the use and measurement of radioactivity	Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland; 1974; Warsaw Institute of Technology; 1968-71 AttoChrom/BioTraces; 1994-96	9 24	20	 100
Biological effects of radiation	Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland; 1974; Warsaw Institute of Technology; 1968-71 AttoChrom/BioTraces; 1994-96	14 24	20	 60

2. Dr. Roman Bielski is the Radiation Safety Officer (RSO) of AttoChrom. Details of Dr. Bielski's radiation training are shown above. Dr. Bielski's work with radioisotopes included synthesis and chromatography of organic compounds containing tritium and iodine-125. The details are shown below:

Radioisotope	Time period	Place	Amount
tritium (^{3}H)	1974-5	Warsaw, Poland	250 microcurie
iodine-125 (^{125}I)	1994-6	Bethlehem, PA	below 1 microcurie
iodine-125 (^{125}I)	1995	NIST, MD	below 1 microcurie (under CRADA between BioTraces and NIST)

3. The duties of the Radiation Safety Officer (RSO) of AttoChrom are:

a. To assess radiological hazards and prescribe, and ensure the implementation of,

appropriate radiation safety precautions.

b. To ensure that the licensed material is under direct supervision of the RSO.

c. To ensure that all the users wear personnel monitoring equipment during iodinations.

d. To ensure that the licensed materials are properly secured against unauthorized removal at all times.

e. To perform routine inspections of both laboratories using or storing licensed materials.

f. To ensure that the terms and conditions of the license are met, and that all required records are maintained.

4. The Radiation Safety Officer, Dr. Roman Bielski, has direct access to the AttoChrom division VicePresident, Richard Wadiak on an as needed basis and they typically meet several times a week. The RSO is responsible to conduct all the necessary inspections within AttoChrom to ensure the requirements of the license. He will control the log books, orders, use, waste disposal and monitoring of necessary bioassays and perform the wipe tests concerning radioactivity.

5. At this point AttoChrom division consists of three employees. Of these, only Dr. Bielski is authorized to handle radioactive materials above exempt amounts. He is the only person from AttoChrom who will have the key to the radio iodination hood room in Iacocca Hall where the radioactive synthesis will be performed. No ancillary personnel will have access to the radio iodination room (C-260). Ancillary personnel working in room 136 of Jordan Hall will be required to attend an appropriate local training program in accordance with NRC requirements which will be developed by Dr. Bielski. Retraining will take place once a year. Every employee will sign an appropriate form showing that (s)he understands and is aware of the rules and will comply with them Part of room 136 in Jordan Hall has been separated from the rest of this facility as an area where radioactive materials and radioactive waste will be stored. This area is well signed and no ancillary personnel is ever allowed to enter this area.

6. Most of the licensed material will be stored in Room C-260, Iaccoca Hall, Lehigh University, in the iodination fume hood room, which is locked at all times. This room is equipped with an appropriate, certified fume hood. We plan to install our own (AttoChrom) locked storage box, where we will store all the licensed material. Only the RSO will have access to this locked box. An appropriate log book will assure that the licensed material is well distinguishable from any radioactive material belonging to Lehigh University.

Significantly smaller amounts of licensed material will be stored in room 136, Jordan Hall (115 Research Dr, Ben Franklin Technology Center, Room 136, Bethlehem, PA 18015). This licensed material will be kept in a locked cabinet and in a locked storage box in the refrigerator, which is used only for storage of biological and radioactive material. Only Dr. Bielski will have keys to this cabinet and box. Also, we plan to chromatograph and measure amounts below 1 nanocurie of radioactivity in the NIST facilities in Gaithersburg, MD. These minute amounts of radioactivity will be transported under our license.

7. The licensed material will be stored and used in the radio-iodination fume hood room C-260, Iaccoca Hall, Lehigh University. It has been approved already by NRC for use of higher amounts

of iodine-125. It is equipped with an appropriate fume hood (recently measured average face velocity - 122,7 FPM) with charcoal bank and is constantly monitored.

Smaller amounts of the licensed material will be used (chromatographed and measured using multi photon detector - MPD) in room 136, Jordan Hall, BFTC, 115 Research Drive, Bethlehem, PA 18015. This room is equipped with the standard fume hood. Additionally, to minimize the effect of radio-isotopes present in the room on MPD measurements we will purchase PVC-coated lead sheets (Instruments for Research and Industry, Inc., P.O. Box 159D, Chaltenham, PA 19012).

8. See enclosed diagrams.

9. We are purchasing one portable meter (Johnson GSM-115 with a GLE-1 probe) from Johnson and Associates, Inc. PO Box 472, Ronceverte, WV 24970. It will be shipped to Anthony LaMastra (Health Physics Associates, 1005 Old Route 22, Lenhartsville, PA 19534, license number 37-28246-01) for calibration, and then sent directly to AttoCi:rom.

10. The portable instrument as described above will be used as a survey instrument to detect iodine-125 contamination. It contains a thin sodium iodide crystal probe and has been selected due to its sensitivity.

11. The calibration will be performed once a year by a Certified Health Physicist -Anthony LaMastra (Health Physics Associates, 1005 Old Route 22, Lenhartsville, PA 19534, license number 37-28246-01).

12. According to Regulatory Guide 8.20 C.c bioassays are not required when process quantities are handled by a worker are less than 10% of those in Table 1. We will not use amounts exceeding 10% of those in Table 1. Therefore, we do not need to establish any bioassay program. However, the activity in the thyroid will be determined after every iodination using the instrument described above. During iodinations this portable device will be kept in the iodination room. It will be calibrated by Anthony LaMastra (Health Physics Associates, 1005 Old Route 22, Lenhartsville, PA 19534, license number 37-28246-01).

13. We confirm that we will periodically (twice a year) calibrate the instrumentation used for determining activity in the thyroid using a neck phantom.

14. We do not expect to generate airborne radioactivity in quantities that would cause a detectable dose to individuals. Our needs require usually pCi to 1uCi activities. We will not be conducting iodinations that are chemically likely to create elemental iodine or other forms that are likely to volatilize.

The ALI (ingestion) concentration is 2×10^{2} uCi. This is two orders of magnitude above what we plan to be handling at any one time. The DAC is 3×10^{-8} uCi/mL. Even if 1 microcurie were to volatilize, it would create a static air concentration in the hood volume of 5×10^{-7} uCi/mL. Since there is constant air flow in the hood of about 400 CFM, the DAC would be achieved in less than 3 minutes. Emergency procedures will state that should a spill occur, the worker is to close the hood

and vacate the hood room. Thus, it is very unlikely that a worker would receive even a small percentage of the occupational dose limits. The instrument described in items 9 and 10 will be used as a real time monitor during iodinations to determine external gamma measurements as required by 20. 1203.

With respect to 20. 1204, should a spill occur, a thyroid scan will be made with the instrument described in items 9 and 10. If the instrument shows measurements exceeding background (plus 3 standard deviations), the worker will be brought to St. Luke's Hospital in Bethlehem, PA for an accurate internal dose assessment.

With respect to 20. 1302, the hood in which all chemical synthesis with iodine is performed is in a locked room within a locked laboratory that is used for radioactive work. Personnel in the hood room are only occupationally exposed. A charcoal filter in the hood exhaust pipe collects any volatilized iodine that might occur. Charcoal canisters are used during iodination activities to determine the air concentrations in the hood. In the past, other iodination work showed that iodine concentrations in the hood were more than two orders of magnitude lower than the air concentration DAC. Should the iodine volatilize, a 5 minute air flow through the hood would create a dilution that was below the air effluent concentration of 3×10^{-10} uCi/mL.

Additionally, we want to emphasize that we do not plan to conduct reactions producing volatile, elemental iodine-125. As we explained in our application, AttoChrom was formed to engage in research and development and, eventually, commercialization of ultra-sensitive MPD (multi photon detection) technology applied to chromatographic separation. The amounts we plan to measure are almost always below the natural radioactive background. The only situation in which higher amounts of radio-iodine-125 are needed is when we synthesize appropriate derivatizing agents (radiophores). These radiophores, after conjugation with the mixture components, enable detection using MPD. The selected radiophores are not natural compounds and their structure can be designed in such a way to make the synthesis safe and relatively easy.

Most synthesis of compounds containing iodine proceed by aromatic electrophilic substitution. For example, one of the protein forming amino acids is tyrosine, which contains electron rich (due to the presence of hydroxy group) aromatic ring. This amino acid can be easily radio-iodinated using iodide (iodine in the form of an anion) and appropriate oxidizing agent such as chloramine T. Oxidation transforms the ion into the neutral atom. Two atoms combine to form a molecule which can engage in aromatic electrophilic substitution. Unfortunately, iodine molecules are highly volatile and can enter the human body and, eventually, the thyroid as the result of breathing air containing iodine.

We want to emphasize that we do not intend to ever perform radio iodinations in the presence of an oxidizing agent. However, we do consider using derivatizing agents (radiophores) which can be synthesized via radio-iodination in the presence of oxidizing agents. We have initiated a collaboration with ICN Biologicals, Inc., in regard to such synthesis. We will perform "cold" synthesis and supply ICN Biologicals with appropriate chemicals and they will synthesize the "hot" product.

The radioiodine atoms are often introduced to the aromatic ring of organic molecules as the result of nucleophilic substitution of halogen (bromine or iodine atom). This reaction requires relatively

high temperature (above 100°C) and is carried out in the presence of copper (I) salts. Radioactive yields are high and no oxidation is needed. We plan to use mostly this process in our synthetic efforts. Additionally, we may use the Sandmeyer reaction (diazonium salts transformation to compounds with radio-iodine atoms in the aromatic ring) and its modifications.

15. The bioassay program of AttoChrom includes thyroid measurements after every iodination using the portable instrument described in item 9. Similar bioassays will be performed monthly for every worker who works (temporarily or permanently) in room C-260, Iaccoca Hall. Additionally, persons employed in this room will have their urine samples measured 4 times a year using the Beckman instrument (5500) in the room C-232 in Iaccoca Hall. The records of urine and thyroid measurements will be kept and will be always available for inspection. If positive results are obtained, *i.e.* measurements exceeding background (plus 3 standard deviations), the worker will be brought to St. Luke's Hospital for an accurate internal dose assessment. However, since we intend to use only small amounts of licensed material in our synthetic work we do not have to have any bioassay procedures.

16. See enclosed instruction (Safety instruction for iodination).

17. AttoChrom is extremely concerned with any contamination by radioactive materials not only for obvious safety reasons but also because ultra-high sensitivity of MPD technique is based on almost perfect rejection of radioactive events of no interest. We cannot afford to contaminate our measuring devices. Therefore, our survey program will be performed after every use of the radio-iodination room. We will wipe every part of the used glassware and hood which can be contaminated, and measure these samples for 5 minutes using the Beckman instrument (5500) in room C-232 (Iaccoca Hall). Any measurement exceeding the natural background by 20 % as measured by the same instrument will be considered contamination. All such measurement records will be maintained.

18. At this point, we do not anticipate to work with amounts higher than a few microcurie of iodine-125. As already mentioned, each wipe sample will be measured using the Beckman gamma counter in room C-232. In case of contamination higher than 20 % above the background we will clean the glassware used and also the surface and walls of the hood with an appropriate absorbant. The resulting waste will be stored in the hood until it shows no radiation above the natural background (Beckman 5500). If a thyroid survey with the portable Johnson GSM-115 meter shows measurement exceeding background (plus 3 standard deviations), the worker will be brought to St. Luke's Hospital for an accurate internal dose assessment.

19. See enclosed instruction (Handling of Radioactive Material).

20. Licensed material will be stored in room C-260 of Iacocca Hall which has restricted access and a cipher lock. Only people knowing the cipher code can enter the room. Part of this room is the radio iodination hood room with a door ,which is always locked. Only Dr. Bielski will have access to this room. Presently, no Lehigh University researchers use this facility. We do not anticipate non-instructed personnel to ever have access to this area. Nevertheless, we will keep AttoChrom's

radioactive materials in a locked safety cabinet within this room.

Significantly smaller amounts of radioactivity will be kept in room 136, Jordan Hall. They will be also kept in a locked safety cabinet and in a locked safety box in the refrigerator.

21. Since we plan to work with small amounts of radioactive material and we do not expect to use the radio iodination hood more often then once or twicea month, we plan to use personnel monitoring devices which will be checked quarterly. We will purchase TLD badges from Landauer Inc., 2 Science Road, Glenwood, Il 60425-1586. Roman Bielski is the only person to work with non-exempt amounts of radioactivity.

22. Since we will use extremely small amounts of radioactivity in a single experiment, internal monitoring does not seem to be necessary. However, we will take urine samples from workers working in the radio-iodination room every three months and measure these samples using the Beckman5500 instrument. If the reading exceeds background (plus three standard deviations) the worker will be brought to St. Luke's Hospital for accurate internal dose assessment.

23. The only radio-isotope we ask the license for is iodine-125. We plan to buy this radio-isotope almost exclusively in the form of iodide ions in solution. We will keep a log book in the AttoChron facility (Jordan Hall, room 136). We will also maintain a log book in the radio-iodination room in Iacocca Hall (room C-260). We do not anticipate storing radioactive material in other locations. We will monitor the amounts ordered and received against those already present. We will check the materials and compounds to assign them new radioactivity levels due to radioactive decay (half live of ^{125}I isotope is 60 days) on a quarterly basis. These calculations will be supported by appropriate measurements using MPD instruments.

24. We confirm that radioactive waste, held for decay-in-storage will be:

- held a minimum of ten half-lives which, in the case of ^{125}I, is equal to 600 days;
- monitored prior to disposal, and then
- disposed as ordinary trash only if the radiation levels are at background.

25. Most compounds we plan to synthesize are not known compounds. However, any "hot" synthesis will be preceeded by a "cold" synthesis. Therefore, we will have available non-radioactive equivalents of all the compounds of interest. We will determine experimentally if the compound is "readily soluble" as defined in NRC Information Notice 94-07. Nevertheless, **we will not dispose of any radioactive material into sanitary sewerage.**

26. We will maintain records of the following activities:

- results of audits and surveys performed by the Radiation safety officer,
- decay-in-storage waste records, including the date licensed material is placed into storage, and the date and results of surveys performed when disposed,
- receipt and transfer of licensed material,

- licensed material inventory,
- calibration of radiation monitoring instruments and equipment,
- initial and refresher radiation safety training of personnel.

27. We will post the names of the persons to be contacted in the case of an emergency. Since we are concerned with an extremely sensitive detection method, even for radiophore synthesis we will use small amounts of radio-iodine. Thus, the risk of a major spill is rather limited. Nevertheless, we have established appropriate procedures. The copy of our emergency procedure is enclosed (Emergency Procedures).

28. Dr. Bielski is the only person in AttoChrom responsible for ordering radioactive materials. Before ordering he will check the log books to verify that the licensed amount will not be exceeded. However, it should be emphasized that we plan to use and store amounts significantly lower than 5 millicurie (the amount we ask the license for). Upon receipt of licensed material in Jordan Hall it will be examined using the portable counter for potential leaks. If no radioactivity is detected from outside of the package, it will be transported to the room C-260 (radio iodination hood room). We will require the suppliers we buy radioactive material from to notify us in advance about the method and time of shipping. This will enable the designated person, Dr. Bielski, to be present when the parcel arrives.

29. The received package will be first examined for leakage or contamination. Next, it will be transported to the radio iodination room. There and only there packages will be opened using all the appropriate precautions (hood, gloves, mask if necessary, lead shield and so on). We will establish written procedures for safely opening packages with radioactive material in accordance with 10 CFR 20.1906.

30. The appropriate letter signed by BioTraces President - Dr. E. James Wadiak has been sent to the NRC.

Additionally, we would like to amend our application to the NRC. In our Application for Material License, AttoChrom anticipated that its employees would attend the Radiation Safety Training Sessions conducted by Lehigh University for its employees. Due to a misunderstanding on my part, this service will not be available to AttoChrom. Lehigh University does not conduct training for researchers who are not faculty or students of the Lehigh University. Therefore, we will conduct our own employee training.

Our Radiation Safety Training Program will consist of visual aids explaining the background, potential health risks of radioactivity and appropriate safety precautions. The training focuses on the specific isotopes used in our research at AttoChrom. However, it should be pointed out that Roman Bielski is the only person who will have access to amounts of licensed material above the exempt amount.

Since this is a deviation from what was stated in the original application, we would like to add an amendment concerning employee training and waste disposal procedures.

Amendment:

Item 7: Delete second sentence in paragraph 1.

Item 8 should read as follows: AttoChrom has developed its own program of employee training. All the employees are required to attend this training.

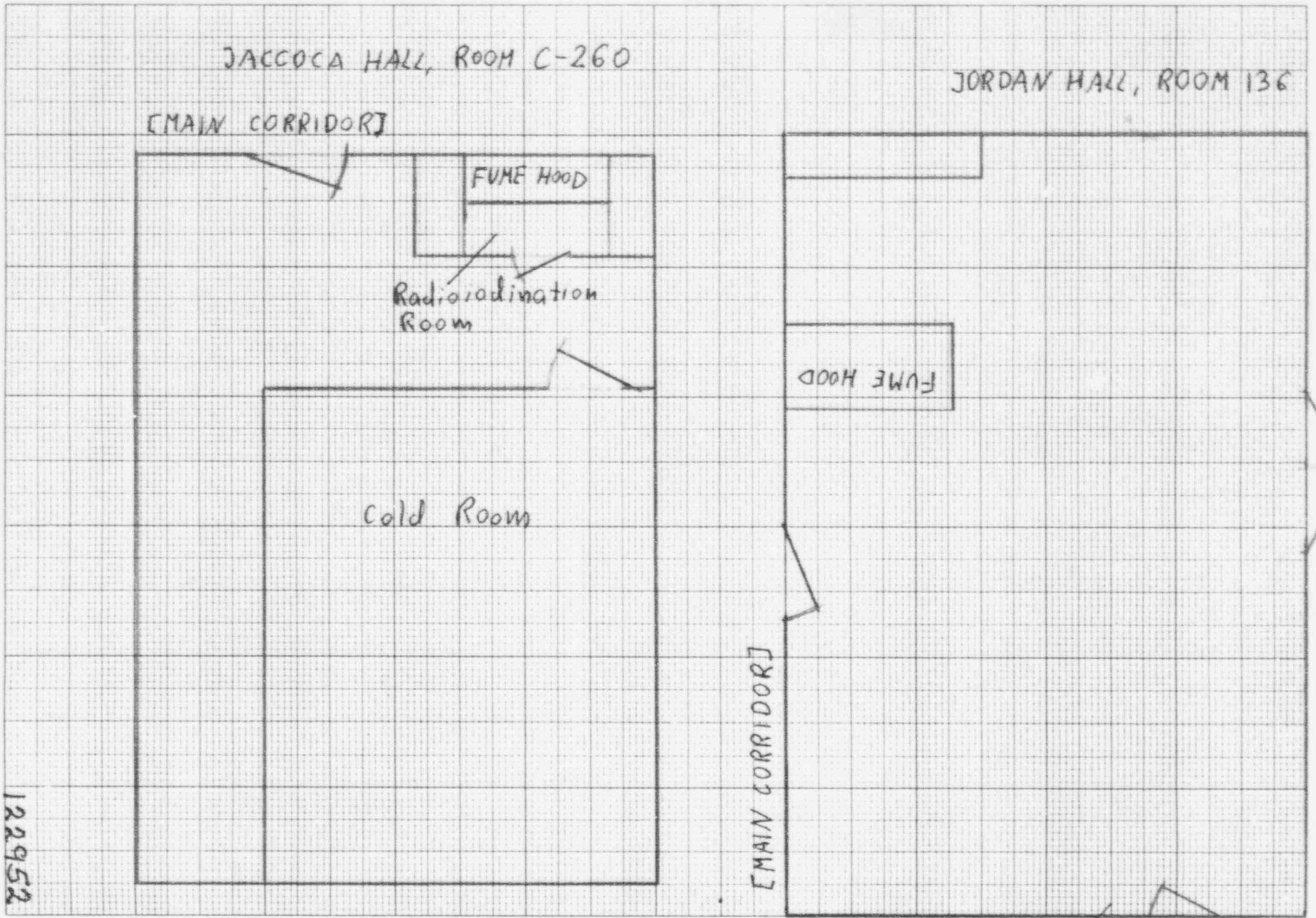
Item 10: Delete first sentence. Add: AttoChrom is developing its own safety program in accordance with the NRC requirements.

Item 11: Delete the statement "We will follow all the requirements of Lehigh University".

If you need any additional information do not hesitate to call us.

Yours sincerely,

Roman Bielski



122952

1cm = 0.5m

ATTOCHROM/BIOTRACES, INC.

Safety instruction for iodination (room C-260)

1. Iodinations will be performed only inside of the closed hood. They should be always preceded by the "cold" run if possible.

2. The locked box with licensed material will not be removed from the radio-iodination fume hood.

3. After each iodination the thyroid test with the portable Johnson GSM-115 counter with a GLE-1 probe has to be performed. The result has to be recorded in the provided record book.

4. A wipe test of two randomly selected fume hood spots plus outside of the reaction flask (area of about 300 cm^2, moderate pressure) must be performed. Next, the absorbent material will be measured in the room C-232 using the Beckman counter 5500. The results must be recorded in the provided record book.

Handling of Radioactive Material

Each Authorized User must enforce compliance with the following regulations and procedures by all personnel under his/her supervision.

1. Personal Contamination

   a. Before any work is undertaken with quantities of radionuclides which may produce significant external or internal exposure, attention must be given by the user to precautionary measures including the use of hoods, remote handling equipment and air monitoring.

   b. Work shall be planned carefully to minimize any chance of spilling radioactive materials. Good housekeeping is encouraged at all times.

   c. Smoking, drinking, eating, applying of cosmetics and storing or preparation of food is prohibited in radioisotope laboratories.

   d. No radioactive materials shall be pipetted by mouth. Automatic pipetting devices or rubber bulbs should be used.

   e. Personnel are not permitted to work with radioisotopes if there are open cuts or abrasions on exposed areas of the body. Extreme precautions must be taken to avoid cuts or puncture wounds.

   f. Care must be exercised when using organic solvents to avoid skin contact with radioactive materials (Solvents may make the skin more permeable).

   g. Laboratory coats should be worn by all individuals handling radioactivity and should be removed before leaving the laboratory. Clothing should be monitored for contamination before leaving the area.

   h. Rubber or plastic disposable gloves should be worn when handling containers of radioactive material.

   i. Monitoring equipment must be available and in operating condition at all times and used frequently during and following work to determine the presence of activity and contamination on hands, clothing and facilities. Each user is personally responsible to check himself or herself (hands, feet, clothing) for contamination <u>each and every time</u> he/she has run a risk of contamination.

   j. Any person who knowingly swallows, inhales or otherwise ingests radioactive material must report the accident <u>immediately</u> to the University Radiation Safety Officer or his/her representative at the Office of Risk Management/Environmental Health and Safety.

k. When using radioactive material that is in a volatile state or becomes volatile at some point in the procedure, work should be carried out in a ventilated fume hood.

2. Contamination of Laboratory Equipment, Glassware and Surfaces

a. Handling tools and equipment, when used and considered contaminated, should be placed in non-porous metal trays or pans located off to one side, away from the actual working place. It is desirable to line such trays and pans with absorbent disposable paper, which should be changed frequently. These papers should be regarded as radioactive waste only when surveys indicate activity above background or when known contamination occurs.

b. Auxiliary containers, absorbent paper and container lids or stoppers shall always be used where danger of spills and contamination of the user or equipment is possible.

c. A caution label or sticker shall be affixed on all containers and equipment that are contaminated with radioactivity until cleaning can be performed. These labels or stickers are available from commercial suppliers.

d. Removable contamination shall not be allowed to remain on floors, bench tops or other facilities (e.g., refrigerators, hoods, etc.). Where floors are known to be or suspected of being contaminated, the area involved shall be immediately restricted to further traffic and designated as a shoe cover area until such time as it is shown to be free of removable contamination.

When bench tops or other equipment is known to be contaminated, cleaning shall be undertaken immediately until it is shown to be free of removable contamination.

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Emergency Procedures

In the event of an emergency or suspected emergency (a major spill, overexposure, etc.), The Radiation Safety Officer (RSO) shall be notified immediately without such actions to cause excessive spread of contamination. **TELEPHONE NUMBERS:**
Dr. Roman Bielski, (610) 861-6948 (AttoChrom); (610) 967-9754 (home)

The user shall be responsible for the decontamination procedures necessary and shall carry out these procedures under the direction of the Radiation safety Officer or persons designated by him.

1. Minor spills - involving no significant radiation hazard to personnel:

    a. Notify all other persons in the area **at once**.

    b. Permit only the minimum number of persons necessary to deal with the spill into the area.

    c. Immediately confine minor spills.

        1. Liquid spills - Don protective gloves and footwear.
        - Drop absorbent paper on spill.

        2. Dry spills - Don protective gloves and footwear.
        - Gently dampen the area thoroughly and cover it with absorbent paper taking care not to spread the contamination.

        3. Dispose of damp towels in the labeled radioactive waste container.

        4. Monitor the area with a low-level survey meter and wipe tests to determine the effectiveness of the decontamination.

    d. Notify the Radiation Safety Officer as soon as possible, giving all details of the spill.

2. Major spills - involving radiation hazard to personnel:

    a. Notify all persons not involved in the spill to vacate the room at once.

b. Check to make sure shoes are not contaminated with radioactivity.

c. Make no immediate attempt to clean up the spill.

   1. If the spill is liquid and the hands are protected, right the overturned container.

   2. If the spill is on the skin, flush thoroughly with water. Do not scrub or use strong detergents.

   3. If spill is on street clothing, go to the men's/ladies' room and remove all wet clothing, wash the affected skin area, monitor and put on clean, dry clothing. Save personal clothing in plastic bags in case the employee wants it cleaned and returned.

d. Switch off all fans and air conditioners.

e. Vacate the room and prohibit unauthorized entrance to the contaminated area by posting the area with a warning sign.

f. Notify the Radiation Safety Officer and the Authorized User at once, giving all details of the accident.

g. The spread of radioactive contamination can be diminished by restricting the movements of potentially contaminated persons to a local zone just outside of the spill area until the extent of shoe and clothing contamination is ascertained.

h. Anyone who might have been contaminated should be monitored for radioactivity and, if contaminated, should discard that clothing and be decontaminated. If no means are available for monitoring, it should be assumed that the person is contaminated.

i. Immediately take the necessary steps to decontaminate personnel involved. Under no circumstances should an untrained person attempt to examine or clean up the radioactive material.

j. Decontaminate the area under the supervision of the Radiation Safety Officer or his/her designate.

k. Monitor all persons involved in the spill and cleaning to determine the effectiveness of decontamination.

l. If personnel contamination has occurred from a major radioactive material spill, a bioassay may be required. The RSO and attending physician will make the assessment.

m. Permit no person to resume work in the area until a survey is made and written approval of the Radiation Safety Officer or his/he. designee is obtained.

3. Accidents involving radioactive dusts, mists fumes, organic vapors and/or gases:

   a. Notify all other persons to vacate the room immediately.

   b. Hold breath and switch off air-circulating devices if possible and if time permits.

   c. Vacate the room.

   d. Monitor all persons and the area suspected of contamination and, if contaminated, decontaminate.

   e. Notify the Radiation Safety Officer and the Authorized User at once, giving all details of the accident.

   f. Ascertain that all doors giving access to the room are closed and sealed with wide masking tape or adhesive tape and heavy paper. Post conspicuous warning signs or guards to prevent accidental opening of doors.

   g. Report at once all known or suspected inhalations of radioactive materials.

   h. Decontaminate the area under the supervision of the Radiation Safety Officer or his/her designee.

4. Injuries to personnel involving radiation hazards:

   a. Wash minor wounds immediately under running water while spreading the edges of the wound.

   b. Seek medical advice, informing the physician of the nature of the injury, the radionuclide and the potential activity involved.

   c. Report all radiation accidents (wounds, overexposures, ingestion, inhalation, etc.) to the Radiation Safety Officer as soon as possible.

   d. Permit no person involved in a radiation injury to return to work without the approval of the Radiation Safety Officer and the attending physician.

e. Have appropriate bioassays performed as specified by the Radiation Safety Officer and/or the attending physician.

5. Fires involving radioactive material:

a. Notify all persons in the room and building at once.

b. Notify the fire department and Radiation Safety Officer of the emergency involving radioactive material and the potential hazard.

c. Attempt to put out minor fires if radiation hazard is not immediately present.

ATTOCHROM

Division of BioTraces, Inc.

115 Research Drive
Bethlehem, PA 18015-4734

tel: (610) 861-6948
fax: (610) 861-8247

June 7, 1996

Dr. Elizabeth Ulrich, Senior Health Physicist
Nuclear Materials Safety Branch 2
Division of Nuclear Materials Safety
United States Nuclear Regulatory Commission
Region 1
475 Allendale Road
King of Prussia, PA 19406-1415

Re: Application to US Nuclear Regulatory Commission, Mail Control Number 122952

Dear Dr. Ulrich,

We have not yet completed our response to your letter dated May 10, 1996 to Dr. Roman Bielski at the AttoChrom division of BioTraces, Inc. Unfortunately, your letter was not received in our office until May 21. Additionally, Dr. Bielski was traveling several days during the intervening period.

Therefore, we respectively request a 10-day extension, so that we have the opportunity to provide comprehensive answers to all your questions.

Please feel free to contact either Dr. Bielski or myself concerning this extension request at 610 - 861-6948.

Sincerely,

Richard A. Wadiak
Vice President
AttoChrom division of
BioTraces, Inc.

6-11-96

MAY 10 1996

Docket No. 030-34088
Control No. 122952

Roman Bielski, Ph.D.
Attochrom/Biotraces, Inc.,
115 Research Drive, Suite 136
Ben Franklin Technology Center
Bethlehem, PA 18015

Dear Dr. Bielski:

This is in reference to your application for NRC license. In order to continue our review, we need the following additional information:

1. Provide a brief resume of the training and experience of each person who will directly supervise the use of material, who will use material without supervision, or who will have responsibility for radiological safety. The resume should include the type (on-the-job or formal course work), location, and duration of the training. Training should cover (a) principles and practices of radiation protection, (b) radioactivity measurements, standardization, and monitoring techniques and instruments, (c) mathematics and calculations basic to the use and measurement of radioactivity, and (d) biological effects of radiation. The description of the use of licensed materials should include the specific isotopes handled, the maximum quantities of materials handled, where the experience was gained, the duration of experience, and the type of use.

2. Identify the individual who will be the Radiation Safety Officer (RSO) on your license. Please describe this individual's formal training in the following areas:

   a. principles and practices of radiation protection;

   b. radioactivity measurements standardization and monitoring techniques and instruments;

   c. mathematics and calculations basic to the use and measurement of radioactivity; and

   d. biological effects of radiation.

   In addition, describe the specific isotopes the individual has handled, the maximum quantities of materials handled, where the experience was gained, the duration of the experience and the type of use.

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ML 10

3. Submit a description of the duties and responsibilities of your Radiation Safety Officer. The typical duties of a Radiation Safety Officer would be:

   a. To assess radiological hazards and prescribe, and ensure the implementation of, appropriate radiation safety precautions.

   b. To ensure that the use of licensed material is by or under the direct supervision of individuals specifically listed on your license.

   c. To ensure that all users (where appropriate) wear personnel monitoring equipment when using licensed materials.

   d. To ensure that licensed materials are properly secured against unauthorized removal at all times when not in use.

   e. To perform routine inspections of all laboratories using or storing licensed materials.

   f. To ensure that the terms and conditions of your license are met, and that all required records are maintained.

4. Provide a description or an organizational chart which shows that the Radiation Safety Officer has a direct reporting path to senior management. Also provide a statement delineating the Radiation Safety Officer duties and responsibilities for carrying out the radiation safety program.

5. In your application, you didn't describe a training program for ancillary personnel (maintenance, security, etc.) and personnel involved in radionuclide work. Please describe a program that will:

   a. be of sufficient scope to ensure that all personnel using licensed materials, or frequenting areas where licensed materials are used, receive proper instruction in accordance with 10 CFR 19.12 (enclosed);

   b. assure that personnel are instructed before assuming duties with, or in the vicinity of, licensed materials with retraining as necessary;

   c. specify a frequency for retraining.

   The training given to each group should be commensurate with the duties and responsibilities of the group and need not be the same for each group.

6. Please provide addresses of all locations where you plan to use/store licensed material. Your application indicates that licensed material may be used at the facilities of Lehigh University, and National Institute of

Standards and Technology (NIST). Because these facilities also have NRC licenses to possess and use byproduct material, provide details of how you plan to keep your licensed activities separated from those of Lehigh University and NIST.

7. Describe the facilities and equipment (e.g., remote handling equipment, storage containers, shielding, fume hoods) to be made available at each location where licensed material will be used. Submit a description of the areas assigned for the receipt, storage, preparation, and measurement of licensed materials. Submit a diagram showing the locations of shielding, the proximity of radiation sources to unrestricted areas, and other items related to radiation safety. For facilities where licensed materials may become airborne, include schematic descriptions of the ventilation system, with pertinent airflow rates, pressures, filtration equipment, and monitoring instruments. Diagrams should be drawn to a specified scale, or dimensions should be indicated.

8. Provide diagrams of facilities designed or established for the use of radioisotopes, including the iodination laboratories.

9. You must have at least one portable radiation monitoring instrument that is capable of making quantitative measurements required for such activities as: radiation level measurements of packages prior to transportation; package receipt surveys; incidents; and assuring that radiation levels in unrestricted areas are in compliance with NRC regulations. Specify the number and types of instruments you will have available for quantitative radiation level measurements, which should be appropriate for the types and quantities of materials requested on your license application.

10. Your equipment should include a survey instrument with a thin sodium iodide crystal detector probe to detect iodine-125 contamination. Please specify the instrument that will be used for this purpose.

11. Specify the calibration method, and confirm that the instrument(s) will be calibrated at least once every twelve months. If you intend to contract out the calibration of your instruments, you only need to specify the name of the firm and the license number that authorizes the firm to perform calibration services.

12. Your application did not specify the instrument used in your bioassay program for determining activity in the thyroid. Please specify your instrumentation and calibration procedures, including the type of phantom you will use.

13. Your application didn't describe the calibration of the instrument used for thyroid bioassay counts. Confirm that you will periodically calibrate the instrumentation used for determining activity in the thyroid using a neck phantom.

14. Describe your procedures for complying with Sections 20.1203, 20.1204, and 20.1302 of 10 CFR Part 20, for procedures such as iodinations that may release volatile or gaseous radioactive materials to restricted and unrestricted areas. You should include a description of the type of surveys (e.g., environmental or breathing zone), frequency of surveys, and the individuals who will perform the surveys (e.g., radiation safety officer or investigator), equipment to be used, and the procedures for evaluating the results.

15. Describe your bioassay program, including the type of bioassay (thyroid counts, urine counts, whole body counts, etc), the criteria and the frequency for performing bioassays, and the type of action taken when positive results are obtained. It is recommended that bioassay procedures be considered for personnel using millicurie quantities of tritiated organic compounds, iodine-131, and iodine-125 in noncontained forms.

16. In support of your request for more than one millicurie of radioiodine, submit special safety instructions to be provided to individuals. Your procedures should include:

    a. A mandatory radiation survey and wipe test for radioactive contamination after each use.

    b. Bioassay procedures for individuals working with millicurie quantities of radioiodine.

    c. The use of vented hoods for iodination and for the storage of millicurie quantities of radioiodine.

    d. A dry run prior to the performance of unfamiliar procedures in order to preclude unexpected complications. In addition, it is recommended that the radiation protection officer be present during new procedures.

    e. Procedures for measuring the concentration of radioiodine from the hoods where material is stored and where iodinations are performed.

17. Provide a more complete description of the routine survey program, including the areas to be surveyed, the types and levels of radiation and contamination considered to be acceptable, and provisions for maintaining records of surveys. The individual user should supplement the surveys performed by the radiation staff. Regularly used laboratories should be surveyed for contamination at the end of each workday (except when quantities less than those in Appendix C to 10 CFR Part 20 are handled by an employee at any one time), and the user should maintain records of each surveys in units required by 10 CFR Part 20, even if only a single measurement is necessary.

18. Specify the action limits for radiation and contamination surveys and the actions to be taken when these limits are exceeded. The action limits should be in appropriate units.

19. Please provide a copy of your laboratory instructions. Typical instructions should include:

    a. Wear laboratory coats or other protective clothing at all times in areas where licensed materials are used.

    b. Wear disposable gloves at all times while handling licensed materials.

    c. Either after each procedure or before leaving the area, monitor your hands for contamination in low-background area.

    d. Do not eat, drink, smoke or apply cosmetics in any area where licensed material is stored or used.

    e. Do not store food, drink or personnel effects in areas where licensed material is stored or used.

    f. Wear required personnel monitoring devices at all times while in areas where licensed materials are used or stored.

    g. Dispose of radioactive waste only in designated, labeled and properly shielded receptacles.

    h. Never pipette by mouth.

    i. Confine radioactive solutions in clearly labeled containers.

    j. Secure all licensed material when not under the constant surveillance and immediate control of the authorized users.

20. 10 CFR 20.1801 requires that licensed material be secured against unauthorized removal from the place of storage. 10 CFR 20.1802 requires that the licensee control and maintain constant surveillance over materials in unrestricted areas that are not in storage. In your application, you did not indicate how you will secure licensed material. Describe how you will preclude the unauthorized removal of licensed material from the place of storage and in unrestricted areas.

21. Specify the criteria used to assign personnel monitoring devices (e.g., film/TLD whole body and extremity badges), state the device processing frequency, and your dosimetry system processor who is required to be NVLAP approved. If direct reading dosimeters will be used, specify the calibration frequency and method.

22. Specify your criteria for performing internal monitoring which may be required for uses of material under your license. Submit a description of procedures, including the methods and instrumentation to be used for sampling and analysis, calibration of equipment, the lower limit of detection for the method and instrumentation, and the action levels for each radionuclide.

23. Describe your licensed material inventory, control and accountability program. Your inventory and control system should have the capability to assure that licensed material possession limits are not exceeded and that material is accountable at any given time.

24. Confirm that radioactive waste, held for decay-in-storage will be:

    (a) held a minimum of ten half-lives,

    (b) monitored prior to disposal, and then

    (c) may be disposed as ordinary trash only if the radiation levels are at background,

25. 10 CFR 20.2003(a)(1) requires that a licensee may discharge licensed material into sanitary sewerage if the material is readily soluble (or is readily dispersible biological material). Information Notice 94-07 (enclosed) provides methods for determining compliance with this requirement which are acceptable to the NRC.

    Please review this Information Notice and provide specific information as to how you will assure that your releases to the sanitary sewerage system will meet the solubility criteria in 10 CFR 20.2003(a)(i). If you wish, you may indicate that you will use one of the methods described in Information Notice 94-07. Otherwise, describe your alternative methodology including the models, calculations, analytical techniques, and quality control measurements as well as the records that will be maintained.

    In addition, provide calculations to show compliance with 10 CFR 20.2003(a)(2)(3)(4) and confirm that records will be maintained of all disposals made into the sanitary sewage system.

26. Confirm that you will maintain records of the following activities:

    a. results of audits and surveys performed by the Radiation Safety Officer or his designee

    b. decay-in-storage waste records, including the date licensed material is placed into storage, and the date and results of surveys performed when disposed

c. receipt and transfer of licensed material

d. licensed material inventory

e. calibration of radiation monitoring instruments and equipment

f. initial and refresher radiation safety training of personnel

27. In your application, no mention was made of establishing and posting emergency procedures. Regulatory Guide 10.7 recommends that licensees establish emergency procedures that address immediate actions to be taken and persons to be contacted (including appropriate phone numbers). Please confirm that you will draft and post a set of emergency procedures. It is recommended that such procedures contain:

a. instructions to be followed during minor spills,

b. instructions to be followed during major spills, and

c. your radiation safety officer's name, office telephone number, and a telephone number to be used during off-hours.

28. Describe your procedures for ordering and receipt of licensed materials, and for notification of responsible persons upon the receipt of these materials.

29. Provide procedures for examining incoming packages for leakage, contamination, or damage and for safely opening packages in accordance with 10 CFR 20.1906. The monitoring should be performed as soon as practicable after receipt of the package of licensed material. The procedures may vary depending upon the quantity of licensed material received, but should, at a minimum, include instructions for surveying packages, wearing gloves while opening packages, and checking packing material for contamination. Even though the regulation exempts certain packages from immediate monitoring, all licensees must have safe opening procedures for all packages containing licensed material in accordance with 10 CFR 20.1906(e).

30. Your application should have been signed by a management representative rather than the researcher. Please submit a letter signed by a management representative indicating that management has reviewed the application and concurs in the statements and representations contained therein. Note also that a management representative should sign all future correspondence which request change in your license.

We will continue our review upon receipt of this information. Please reply in duplicate to my attention at the Region I Office and refer to Mail Control No. 122952. If you have any technical questions regarding this deficiency letter, please call Dr. Sattar Lodhi at (610) 337-5364.

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In order to continue prompt review of your application, we request that you submit your response to this letter within 30 calendar days from the date of this letter.

Sincerely,

Original Signed By:
Elizabeth Ullrich

Elizabeth Ullrich
Senior Health Physicist
Nuclear Materials Safety Branch 2
Division of Nuclear Materials Safety

Docket No. 030-34088
Control No. 122952

Enclosures:
1. 10 CFR Parts 19, 20, 30, and 170
2. Regulatory Guides 8.9, and 10.7
3. Information Notice 94-07

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NAME	SLodhi		EUllrich					
DATE	05/10/96		05/ /96		05/ /96		05/ /96	

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FAX TRANSMITTAL SHEET

BIOTRACES, INC.
10517-A West Drive
Fairfax, VA 22030
703-273-6941
Fax: 703-273-6968

To: Dr. Elizabeth Ulrich **Date:** 6/7/96

Fax #: 610-337-5324 **Pages:** 7 including cover sheet.

From: Richard Wadlak

Subject:

MESSAGE:

ATTOCHROM

Division of BioTraces, Inc.

115 Research Drive
Bethlehem, PA 18015-4734

tel: (610) 861-6948
fax (610) 861-8247

June 7, 1996

Dr. Elizabeth Ulrich, Senior Health Physicist
Nuclear Materials Safety Branch 2
Division of Nuclear Materials Safety
United States Nuclear Regulatory Commission
Region 1
475 Allendale Road
King of Prussia, PA 19406-1415

Re: Application to US Nuclear Regulatory Commission, Mail Control Number 122952

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Sincerely,

Richard A. Wadiak
Vice President
AttoChrom division of
BioTraces, Inc.

LL 30283
030 - 34088
03620

Roman Bielski, Ph.D.,
AttcChrom/BioTraces, Inc.,
115 Research Drive, Suite 136,
Ben Franklin Technology Center, Bethlehem, PA 18015
tel: (610) 861-6948, fax: (610) 861-8247

Bethlehem, 02.09.96

U.S. Nuclear Regulatory Commission, Region I,
Nuclear Materials Safety Section B,
475 Allendale Road, King of Prussia, PA 19406

Dear Sir (Madam):

BioTraces, Inc. is a Company, located in Fairfax, VA, involved in application of its proprietary multi photon detection (MPD) technology to various biological and medical fields. The technology enables ultra-sensitive detection of some radioactive isotopes. It has been documented that for large molecules we can detect and quantify as small concentrations as 1 zeptomole/mL (10^{-21} mole /mL). For several smaller molecules the limit of detection is at the level of attomoles (10^{-18} mole /mL). For example, for ^{125}I we can detect as small quantities as femtoCuries. Potential applications of this unsurpassed sensitivity are numerous. Currently, we try to apply our detectors to the following areas:

- radioimmunoassays,
- genomics and DNA research,
- chromatography.

The ultra-sensitivity of the MPD technology is achieved as the result of using only select families of artificial radio-isotopes producing at least two highly energetic photons at a time (thus the name MPD). Careful energy and pulse shape analysis of the radioactive events enables distinction of events of interest from all other ones and thus rejection of all the events which are not compatible with those of interest. In most applications MPD detectors work much below background radiation. There are about 100 radio elements which are compatible with MPD. Iodine-125, several lanthanides and actinides belong to this category.

AttoChrom is a division of BioTraces, located in Bethlehem, PA, involved in application of MPD technology to detectors for chromatography. We have shown that our detectors are applicable to high performance liquid chromatography (HPLC) and thin layer chromatography (TLC) and the achieved limits of detection for mixtures of several radio-iodinated steroids and radio-iodinated neurotransmitters (belonging to small amines) are in the range of 0.1 -10 attomoles per sample. Additionally, we have shown that our detectors can be applied to quantitation of mixtures containing no radioactive isotopes.

In this case appropriate derivatizing agents containing radio-isotopes compatible with MPD must be used to introduce the radioactive properties to the mixture constituents. The derivatization with these "radiophores" can take place pre- or post-separation. The objective of AttoChrom is to develop and, eventually, produce kits for derivatization for chromatography using MPD detection. It should be strongly emphasized that the amounts of radioactivity we will use in these kits will be significantly below the background radiation. For applications requiring bigger amounts of derivatizing agents we will use mixtures of "cold" and "hot" compounds.

Until now we have used mostly compounds containing ^{125}I. Nevertheless, MPD technique enables simultaneous detection of several different radioisotopes. We call this option - multicolor. In the future we plan to take advantage of multicolor and use different radiophores for various functional groups, containing different radioisotopes. Several lanthanides, actinides, most iodine isotopes and such radioisotopes as ^{22}Na and ^{60}Co are MPD compatible.

The only commercially available compounds which can be regarded as radiophores (derivatizing agents introducing radioactivity into the chromatographed mixture components) are mono and di-iodinated Bolton-Hunter reagent. They have been used extensively for introduction of radioiodine to peptides and proteins but they can be used also for derivatization of various amines. Our preliminary experiments show that a mixture of a few amines can be successfully radio-derivatized and then separated at the level of about 10 attomole/sample. Additionally, we have synthesized "hot" pipsyl chloride (4-iodobenzenesulphonyl chloride) which happened to be useful radiophore applicable to derivatization of amines and alcohols. In the future, we plan to synthesize several derivatizing agents applicable to various functional groups such as carboxylic acid, carbonyl, catechol and so on.

Our laboratory is located in Ben Franklin Technology Center in Bethlehem, which is a part of Lehigh University mountaintop campus. A lab we rent there has the area of about 600 ft^2 and it is equipped with the fume hood, refrigerator, HPLC pumps and three MPD devices. One of the MPD instruments is capable of measuring 9 samples at a time, the other one has an additional sample changer for 12 samples, the third one is capable of measuring TLC plates. These detectors have been compared with detectors at NIST and are as accurate as their standards. Nevertheless, we plan to buy a Geiger counter. Additionally, we have liaison agreement with Lehigh University (Bethlehem), where we can use Center for Molecular Bioscience and Biotechnology facilities including radioactive rooms and fume hoods. BioTraces also collaborate (CRADA) with National Institute of Standard and Technology and we do use some of their facilities.

At this stage iodine-125 is the only radioisotope we use. For various reasons such as stability of the products, ease and safety of handling, ease of synthesis, we want to use radiophores which are aromatic compounds with radioiodine atoms attached to the ring. There are several ways of introducing radioactive iodine into the aromatic ring of the derivatizing agent:

- Sandmeyer and Sandmeyer/Wallach reaction of aromatic amines;
- intermediate introduction of iodine *via* electrophilic substitution;
- Hunsdiecker reaction and/or its modifications;
- introduction of iodine *via* metalloorganic derivatives of tin, thallium and mercury;
- nucleophilic substitution of halogen atom.

It is well known that reactions with iodide ions carried in the presence of even mild oxidizing agents produce elemental iodine which is volatile and, thus, highly hazardous. We anticipate to introduce iodine atoms to the aromatic ring using either Sandmayer reaction and its modifications (formation of diazonium salt followed by reaction with iodide ion) or using nucleophilic substitution of halogen atom with radio-iodide anion. This way we will avoid formation of elemental iodine. This methodology can be applied to the synthesis of all the radiophores we actually consider. It should be emphasized that derivatizing agents are not natural compounds and, therefore, we can select as our target radiophores in such a way that their synthesis can be as safe as possible.

All our syntheses of "hot" compounds will be preceded by syntheses of "cold" equivalents. It is essential not only to optimize the synthetic reactions conditions but also to optimize the conditions of derivatization and of chromatographic separation. Additionally, we often need to use a mixture of "cold" and "hot" derivatizing agents. Thus, "cold" radiophores must be available.

In most of our measurements we use as small amounts of iodine-125 radioactivity as picoCuries. However, sometimes we have to show the limits of linearity and that calls for higher amounts of radioactivity. Our syntheses are and will be carried at the level of about 1 microCurie. Additionally, we use some radio iodinated compounds which are commercially available such as iodinated streptavidine, steroids, angiotensins, insulin and neurotransmitters. Many of these compounds are not available in amounts smaller than 10 or 100 microCuries. Sodium (^{125}I) iodide and the Bolton-Hunter reagent are available in amounts not smaller than 500 microCuries or 1 milliCurie. Therefore, we want to apply for a licence for 5 milliCurie of iodine-125. It would allow us to accept and store packages containing necessary quantities of iodine-125.

I would be very much obliged if you could arrange a meeting with me so I could explain our research results and our strategy in more details. Anyway, if you need any additional information do not hesitate to call us.

Yours sincerely

Roman Bielski

NRC FORM 313 U. S. NUCLEAR REGULATORY COMMISSION

(10-94)
10 CFR 30, 32, 33
34, 35, 36, 39 and 40

APPLICATION FOR MATERIAL LICENSE

APPROVED BY OMB: NO. 3150-0120
EXPIRES 6-30-96

ESTIMATED BURDEN PER RESPONSE TO COMPLY WITH THIS INFORMATION COLLECTION REQUEST: 9 HOURS. SUBMITTAL OF THE APPLICATION IS NECESSARY TO DETERMINE THAT THE APPLICANT IS QUALIFIED AND THAT ADEQUATE PROCEDURES EXIST TO PROTECT THE PUBLIC HEALTH AND SAFETY. FORWARD COMMENTS REGARDING BURDEN ESTIMATE TO THE INFORMATION AND RECORDS MANAGEMENT BRANCH (T-6 F33), U.S. NUCLEAR REGULATORY COMMISSION, WASHINGTON, DC 20555-0001, AND TO THE PAPERWORK REDUCTION PROJECT (3150-0120), OFFICE OF MANAGEMENT AND BUDGET, WASHINGTON, DC 20503.

INSTRUCTIONS: SEE THE APPROPRIATE LICENSE APPLICATION GUIDE FOR DETAILED INSTRUCTIONS FOR COMPLETING APPLICATION. SEND TWO COPIES OF THE ENTIRE COMPLETED APPLICATION TO THE NRC OFFICE SPECIFIED BELOW. LL 34088

APPLICATION FOR DISTRIBUTION OF EXEMPT PRODUCTS FILE APPLICATIONS WITH:

DIVISION OF INDUSTRIAL AND MEDICAL NUCLEAR SAFETY
OFFICE OF NUCLEAR MATERIALS SAFETY AND SAFEGUARDS
U.S. NUCLEAR REGULATORY COMMISSION
WASHINGTON, DC 20555-0001

ALL OTHER PERSONS FILE APPLICATIONS AS FOLLOWS:

IF YOU ARE LOCATED IN:

CONNECTICUT, DELAWARE, DISTRICT OF COLUMBIA, MAINE, MARYLAND, MASSACHUSETTS, NEW HAMPSHIRE, NEW JERSEY, NEW YORK, PENNSYLVANIA, RHODE ISLAND, OR VERMONT, SEND APPLICATIONS TO:

LICENSING ASSISTANT SECTION
NUCLEAR MATERIALS SAFETY BRANCH
U.S. NUCLEAR REGULATORY COMMISSION, REGION I
475 ALLENDALE ROAD
KING OF PRUSSIA, PA 19406-1415

ALABAMA, FLORIDA, GEORGIA, KENTUCKY, MISSISSIPPI, NORTH CAROLINA, PUERTO RICO, SOUTH CAROLINA, TENNESSEE, VIRGINIA, VIRGIN ISLANDS, OR WEST VIRGINIA, SEND APPLICATIONS TO:

NUCLEAR MATERIALS LICENSING SECTION
U.S. NUCLEAR REGULATORY COMMISSION, REGION II
101 MARIETTA STREET, NW, SUITE 2900
ATLANTA, GA 30323-0199

IF YOU ARE LOCATED IN: 030-

ILLINOIS, INDIANA, IOWA, MICHIGAN, MINNESOTA, MISSOURI, OHIO, OR WISCONSIN, SEND APPLICATIONS TO: 03620

MATERIALS LICENSING SECTION
U.S. NUCLEAR REGULATORY COMMISSION, REGION III
801 WARRENVILLE RD.
LISLE, IL 60532-4351

ALASKA, ARIZONA, ARKANSAS, CALIFORNIA, COLORADO, HAWAII, IDAHO, KANSAS, LOUISIANA, MONTANA, NEBRASKA, NEVADA, NEW MEXICO, NORTH DAKOTA, OKLAHOMA, OREGON, PACIFIC TRUST TERRITORIES, SOUTH DAKOTA, TEXAS, UTAH, WASHINGTON, OR WYOMING, SEND APPLICATIONS TO:

NUCLEAR MATERIALS LICENSING SECTION
U.S. NUCLEAR REGULATORY COMMISSION, REGION IV
611 RYAN PLAZA DRIVE, SUITE 400
ARLINGTON, TX 76011-8064

PERSONS LOCATED IN AGREEMENT STATES SEND APPLICATIONS TO THE U.S. NUCLEAR REGULATORY COMMISSION ONLY IF THEY WISH TO POSSESS AND USE LICENSED MATERIAL IN STATES SUBJECT TO U.S. NUCLEAR REGULATORY COMMISSION JURISDICTIONS.

1. THIS IS AN APPLICATION FOR: *(Check appropriate item)*
   - [V] A. NEW LICENSE
   - [ ] B. AMENDMENT TO LICENSE NUMBER _____
   - [ ] C. RENEWAL OF LICENSE NUMBER _____

2. NAME AND MAILING ADDRESS OF APPLICANT *(Include Zip code)*
Roman BIELSKI, Ben Franklin Technology Center, 115 Research Dr.
Bethlehem, PA 18015

3. ADDRESS(ES) WHERE LICENSED MATERIAL WILL BE USED OR POSSESSED
115 RESEARCH DRIVE, Room 136,
BFTC, Jordan Hall, Bethlehem, PA 18015

4. NAME OF PERSON TO BE CONTACTED ABOUT THIS APPLICATION
Roman BIELSKI

TELEPHONE NUMBER
(610) 861-6948

SUBMIT ITEMS 5 THROUGH 11 ON 8-1/2 X 11" PAPER. THE TYPE AND SCOPE OF INFORMATION TO BE PROVIDED IS DESCRIBED IN THE LICENSE APPLICATION GUIDE.

5. RADIOACTIVE MATERIAL
a. Element and mass number; b. chemical and/or physical form; and c. maximum amount which will be possessed at any one time.

6. PURPOSE(S) FOR WHICH LICENSED MATERIAL WILL BE USED.

7. INDIVIDUAL(S) RESPONSIBLE FOR RADIATION SAFETY PROGRAM AND THEIR TRAINING EXPERIENCE.

8. TRAINING FOR INDIVIDUALS WORKING IN OR FREQUENTING RESTRICTED AREAS.

9. FACILITIES AND EQUIPMENT.

10. RADIATION SAFETY PROGRAM.

11. WASTE MANAGEMENT.

12. LICENSEE FEES *(See 10 CFR 170 and Section 170.31)*
FEE CATEGORY 170.31.M
AMOUNT ENCLOSED $ 1500

13. CERTIFICATION. *(Must be completed by applicant)* THE APPLICANT UNDERSTANDS THAT ALL STATEMENTS AND REPRESENTATIONS MADE IN THIS APPLICATION ARE BINDING UPON THE APPLICANT.

THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATION ON BEHALF OF THE APPLICANT NAMED IN ITEM 2, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PARTS 30, 32, 33, 34, 35, 36, 39 AND 40, AND THAT ALL INFORMATION CONTAINED HEREIN IS TRUE AND CORRECT TO THE BEST OF THEIR KNOWLEDGE AND BELIEF.

WARNING: 18 U.S.C. SECTION 1001 ACT OF JUNE 25, 1948 62 STAT. 749 MAKES IT A CRIMINAL OFFENSE TO MAKE A WILLFULLY FALSE STATEMENT OR REPRESENTATION TO ANY DEPARTMENT OR AGENCY OF THE UNITED STATES AS TO ANY MATTER WITHIN ITS JURISDICTION.

CERTIFYING OFFICER -- TYPED/PRINTED NAME AND TITLE	SIGNATURE	DATE
DR ROMAN BIELSKI	Rob Biel	02/09/96

FEB 26 1996

FOR NRC USE ONLY

TYPE OF FEE	FEE LOG	FEE CATEGORY	AMOUNT RECEIVED	CHECK NUMBER	COMMENTS
			$		
APPROVED BY			DATE		122952

NRC FORM 313 (10-94)

OFFICIAL RECORD COPY ML 10

PRINTED ON RECYCLED PAPER

5. RADIOACTIVE MATERIAL:

a: ^{125}I (iodine-125)
b: alkaline sodium iodide-125 solution in water, iodinated and diiodinated Bolton-Hunter reagent, radio-iodinated streptavidin
c: 5 milliCuries

6. PURPOSE FOR WHICH LICENSED MATERIAL WILL BE USED:

Research and Development leading to selection and optimization of radio-derivatizing agents for chromatography. In the future we plan to produce kits for derivatization for chromatographic detectors.

7. INDIVIDUALS RESPONSIBLE FOR RADIATION SAFETY PROGRAM AND THEIR TRAINING EXPERIENCE:

Roman Bielski, Ph.D. in Organic Synthesis from Institute of Organic Chemistry, Polish Academy of Sciences, including synthesis of natural products containing radioisotopes. I will attend Lehigh University training in radioactive safety as soon as possible.

Eugene A. Nau, Ph.D. in Biochemistry; several years experience in radioiodination of various biological macromolecules at Lehigh University; Lehigh University training.

8. TRAINING FOR INDIVIDUALS WORKING IN OR FREQUENTING RESTRICTED AREAS:

We plan that all the individuals working in the room where radioactivity is used will attend appropriate training organized by Lehigh University.

9. FACILITIES AND EQUIPMENT:

Fume hood, three MPD units, two refrigerators.
Liason agreement with Dept of Biological Sciences, Lehigh University to use their facilities including the radioactive room with fume hood and the room with the Beckmann gamma counter.

10. RADIATION SAFETY PROGRAM:

In accordance with all Lehigh University requirements (we are located in the Ben Franklin Technology center at the mountaintop campus of LU). At present, we do keep a log book where all radioactive material entering and leaving the premises is described. At the moment we keep 0.045 microCuries of iodine-125.

11. WASTE MANAGEMENT:

The half life of iodine-125 is relatively short - about 60 days. Therefore we plan to keep all our

samples for the appropriate time until they can be disposed of safely. It must be reminded that most our measurements will be below background radiation. We will follow all the requirements of Lehigh University.

BETWEEN:

LICENSE FEE MANAGEMENT BRANCH, ARM
AND
REGIONAL LICENSING SECTIONS

(FOR LFMS USE)
INFORMATION FROM LTS

PROGRAM CODE: 03620
STATUS CODE: 3
FEE CATEGORY: _____
EXP. DATE: 0
FEE COMMENTS: _____
DECOM FIN ASSUR REQD: _

LICENSE FEE TRANSMITTAL

A. REGION I

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: ATTOCHROM/BIOTRACES, INC.
RECEIVED DATE: 960226
DOCKET NO: 3034088
CONTROL NO.: 122952
LICENSE NO.:
ACTION TYPE: NEW LICENSE

2. FEE ATTACHED ~~$~~
AMOUNT: 1,500.00
CHECK NO.: 2700

3. COMMENTS

SIGNED M. A. Parkins
DATE 3/14/96

B. LICENSE FEE MANAGEMENT BRANCH (CHECK WHEN MILESTONE 03 IS ENTERED / ✓ aen)

1. FEE CATEGORY AND AMOUNT: 3M $1,500

2. CORRECT FEE PAID. APPLICATION MAY BE PROCESSED FOR:
AMENDMENT _____
RENEWAL ✓
LICENSE _____

3. OTHER _____
_____

SIGNED Brenda Bn
DATE 3/18/96

I (96)

Log MAIL
Remitter BIOTRACES, INC.
Check No. 2700
Amount $1,500
Fee Category 3M
Type of Fee All
Date Check Rec'd 3/18/96
Date Completed 3/18/96
By BBrown